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(71) Applicant *(for all designated States except US)*: AMRAD OPERATIONS PTY. LTD. [AU/AU]; 576 Swan Street, Richmond, VIC 3121 (AU).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: CHOO, Kong-Hong, Andy [AU/AU]; 67 Andersons Creek Road, Doncaster East, VIC 3109 (AU). DU SART, Desirée [AU/AU]; 24 Windella Quadrant, Doncaster, VIC 3108 (AU). CANCILLA, Michael, Robert [AU/AU]; 2 Alameda Avenue, Maribyrnong, VIC 3032 (AU).

(74) Agents: HUGHES, E., John, L. et al.; Davies Collison Cave, 1 Little Collins Street, Melbourne, VIC 3000 (AU).

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(54) Title: A NOVEL NUCLEIC ACID MOLECULE

(57) Abstract

The present invention is directed generally to an isolated nucleic acid molecule encompassing a neocentromere or a functional derivative thereof or a latent, synthetic or hybrid form therof and its use *inter alia* in developing a range of eukaryotic artificial chromosomes including mammalian (e.g. human) and non-mammalian artificial chromosomes. Such artificial chromosomes are useful in a range of genetic therapies.

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A NOVEL NUCLEIC ACID MOLECULE

FIELD OF THE INVENTION

The present invention is directed generally to an isolated nucleic acid molecule encompassing a neocentromere or a functional derivative thereof or a latent, synthetic or hybrid form thereof and its use *inter alia* in developing a range of eukaryotic artificial chromosomes including mammalian (e.g. human) and non-mammalian artificial chromosomes. Such artificial chromosomes are useful in a range of genetic therapies.

BACKGROUND OF THE INVENTION

Bibliographic details of the publications referred to by author in this specification are collected at the end of the description.

The rapidly increasing sophistication of recombinant DNA technology is greatly facilitating research and development in the medical and allied health fields. A particularly important area is in mammalian including human genetics and the molecular mechanisms behind some genetic abnormalities. Progress in research in this area has been hampered by the lack of a cloned nucleic acid molecule encompassing a human centromere. The identification and cloning of a human centromere will promote the development of techniques for introducing genes into eukaryotic cells and in particular mammalian including human cells and will be an important asset to gene therapy and the development of a range of genetic diagnostic tests.

The centromere is an essential structure for sister chromatid cohesion and proper chromosomal segregation during mitotic and meiotic cell divisions. The centromere of the budding yeast *Saccharomyces cerevisiae* has been extensively studied and shown to be contained within a relatively short DNA segment of 125 bp that is organized into an 8-bp (CDEI) and 26-bp (CDEIII) domain, separated by a 78- to 87-bp, highly AT-rich, middle (CDEII) domain (Clarke and Carbon, 1985). The centromere of the fission yeast *Schizosaccharomyces pombe* is considerably larger, ranging from 40 to 100 kb, and consists of a central core DNA element of 4 to 7 kb flanked on both sides by inverted repeat units (Steiner *et al.*, 1993). Recently, the

functional DNA components of a higher eukaryotic centromere have been characterized in a minichromosome from *Drosophila melanogaster* and shown to consist of a 220-kb essential core DNA flanked by 200 kb of highly repeated sequences on one side (Murphy and Karpen, 1995).

The mammalian centromere, like the centromeres of all higher eukaryotes studied to date, contains a great abundance of highly repetitive, heterochromatic DNA. For example, a typical human centromere contains 2 to 4 Mb of the 171-bp α-satellite repeat (Wevrick and Willard 1989, 1991; Trowell *et al.*, 1993), plus a smaller and more variable quantity of a 5-bp satellite III DNA (Grady *et al.*, 1992; Trowell *et al.*, 1993). The role of these satellite sequences is presently unclear. Transfection of a cloned 17-kb uninterrupted α-satellite array into cultured simian cells (Haaf *et al.*, 1992) or a 120-kb α-satellite-containing YAC into human and hamster cells (Larin *et al.*, 1994) appear to confer centromere function at the sites of integration. Other workers have analyzed rearranged Y chromosomes (Tyler-Smith *et al.*, 1993), or dissected the centromere of the human Y chromosome with cloned telomeric DNA (Brown *et al.*, 1994) and suggested that 150 to 200 kb of α-satellite DNA plus ~300 kb of adjacent sequences are associated with human centromere function. In addition, a human X-derived minichromosome that retained 2.5 Mb of α-satellite array has been produced by telomere-associated chromosome fragmentation (Farr *et al.*, 1995). In all these studies, it is not known whether non-α-satellite DNA sequences are embedded within the centromeric site and operate independently of, or in concert with, the α-satellite DNA.

In mammals, four constitutive centromere-binding proteins, CENP-A, CENP-B, CENP-C, and CENP-D, have been characterized to varying extents and implicated to have possible direct roles in centromere function. CENP-A, a protein localized to the outer kinetochore domain, is a centromere-specific core histone that shows sequence homology to the histone H3 protein and may serve to differentiate the centromere from the rest of the chromosome at the most fundamental level of chromatin structure - the nucleosome (Sullivan *et al.*, 1994). CENP-B, a protein which associates with the centromeric heterochromatin through its binding to the CENP-B box motif found in primate α-satellite and mouse minor satellite DNA, probably has a role in packaging centromeric heterochromatic DNA - a role which, however, may not be indispensable since the protein is undetectable on the Y chromosome (Pluta *et al.*, 1990) and is found on the

inactive centromeres of dicentric chromosomes (Earnshaw *et al.*, 1989). CENP-C has been shown to be located at the inner kinetochore plate and is postulated to have an essential although yet undetermined centromere function, as seen, for example, from inhibition of mitotic progression following microinjection of anti-CENP-C antibodies into cells (Bernat *et al.*, 1990; Tomkiel *et al.*, 1994) and from its association with the active but not the inactive centromeres of dicentric chromosomes (Earnshaw *et al.*, 1989; Page *et al.*, 1995; Sullivan and Schwartz, 1995). Finally, CENP-D (or RCC1) is a guanine exchange factor that appears to have a general cellular role that is neither specific nor clear for the centromere (Kingwell and Rattner 1987; Bischoff *et al.*, 1990; Dasso, 1993). More recently, a new role for the mammalian centromere as a "marshalling station" for a host of "passenger proteins" (such as INCENPs, MCAK, CENP-E, CENP-F, 3F3/2 antigens, and cytoplasmic dynein), has been recognized (reviewed by Earnshaw and Mackay, 1994, and Pluta *et al.*, 1995). These passenger proteins, whose appearance at the centromere is transient and tightly regulated by the cell cycle, provide vital functions that include motor movement of chromosomes, modulation of spindle dynamics, nuclear organization, intercellular bridge structure and function, sister chromatid cohesion and release, and cytokinesis. At present, except for CENP-B, none of the constitutive or passenger proteins have been demonstrated to bind mammalian centromere DNA directly.

In work leading up to the present invention, the inventors identified in a patient (hereinafter referred to as "BE") an unusual human marker chromosome, mardel 10, which is 100% stable in mitotic division both in patient BE and in established fibroblast and transformed lymphoblast cultures. In accordance with the present invention, a region of the mardel (10) chromosome has been cloned together with the corresponding region from a normal human subject. The nucleic acid molecules cloned contain no substantial α-satellite repeats yet are mitotically stable. The nucleic acid molecules encompass therefore, a new form of centromere referred to herein as a "neocentromere". The identification and cloning of a eukaryotic neocentromere without substantial α-satellite DNA repeat sequences now provides the means of generating a range of eukaryotic artificial chromosomes such as mammalian including human artificial chromosomes with uses in genetic therapy, transgenic plant and animal production and recombinant protein production. A range of diagnostic reagents is now also obtainable using the cloned neocentromere.

SUMMARY OF THE INVENTION

Sequence Identity Numbers (SEQ ID NOs.) for the nucleotide sequences referred to in the specification are defined following the bibliography.

Throughout this specification and the claims which follow, unless the context requires otherwise, the word "comprise", or variations such as "comprises" or "comprising", will be understood to imply the inclusion of a stated integer or group of integers but not the exclusion of any other integer or group of integers.

A fibroblast cell line 920158 carrying the mardel marker chromosome was deposited at the European Collection of Cell Cultures (ECACC), Centre for Applied Microbiology Research, Salisbury, Wiltshire, SP4 0JG, UK on 1 May, 1997 under Accession No. 97051716. Bacterial artificial chromosomes (BACs) carrying portions of the mardel (10) chromosome have also been deposited at ECACC as follows:

BAC/E8-1: deposited on 5 May 1998 under Accession Number 980505016;
BAC/F2-14: deposited on 5 May 1998 under Accession Number 980505017.

A number of human fibrosarcoma cell lines carrying various neocentromeric constructs were deposited at ECACC as described hereafter by Accession Number with the date of deposit in parenthesises.

HT-38	98050704 (7 May 1998)
HT-47	98050705 (7 May 1998)
HT-54	98050706 (7 May 1998)
HT-190	98050707 (7 May 1998)
HT-191	98050708 (7 May 1998).

One aspect of the present invention provides an isolated nucleic acid molecule comprising a sequence of nucleotides derived from a eukaryotic chromosome and encompassing a

neocentromere or a functional derivative synthetic or hybrid form thereof which nucleic acid molecule or its derivatives, synthetic forms or hybrid forms when introduced into a compatible cell is capable of replicating, acting as an extra-chromosomal element and segregating with cell division.

Another aspect of the present invention contemplates a nucleic acid molecule or its chemical equivalent having a tertiary structure which defines a human neocentromere or a functional derivative thereof or a latent, synthetic or hybrid form thereof or its mammalian or non-mammalian homologue.

Yet a further aspect of the present invention is directed to an isolated nucleic acid molecule comprising a sequence of nucleotides encompassing a neocentromere derived from a eukaryotic chromosome, which nucleic acid molecule when introduced into a compatible cell is a replicating, extra-chromosomal element which segregates with cell division.

Still another aspect of the present invention is directed to an isolated nucleic acid molecule having a sequence of nucleotides or their chemical equivalents which directs a conformation defining a human neocentromere or a functional derivative thereof or a latent, synthetic or hybrid form thereof or a mammalian or non-mammalian homologue thereof wherein the neocentromere associates with centromere binding proteins (CENP) -A and CENP-C or antibodies thereto and does not contain substantial α-satellite DNA repeat sequences.

A further aspect of the present invention is directed to an isolated nucleic acid molecule comprising a nucleotide sequence encompassing a neocentromere or a functional derivative, synthetic or hybrid form thereof which when said nucleic acid molecule is in linear form and co-introduced into a cell together with a telomeric sequence, is capable of replicating, remaining as an extra-chromosomal element and segregates with cell division.

Another aspect of the present invention provides an isolated nucleic acid molecule or a derivative, synthetic or hybrid form thereof comprising a sequence of nucleotides:

(i) which directs conformation defining a human neocentromere or a functional derivative

thereof or a latent, synthetic or hybrid form thereof or its mammalian or non-mammalian homologue wherein said neocentromere is capable of associating with CENP-A and CENP-C;

(ii) which contains no substantial α-satellite DNA sequence repeat; and

(iii) which is capable, when introduced into compatible cells, of replication, remaining extra-chromosomal and segregating with cell division.

Even yet another aspect of the present invention is directed to a genetic construct comprising an origin of replication for a eukaryotic cell and a nucleic acid molecule encompassing a human neocentromere or a functional derivative thereof or a latent, synthetic or hybrid form thereof or its mammalian or non-mammalian homologue flanked by telomeric nucleotide sequences functional in the cell in which the genetic construct is to replicate and wherein said genetic construct when introduced into a cell is a replicating, extra-chromosomal element which segregates with cell division.

Another aspect of the present invention is directed to a genetic construct in the form of a eukaryotic artificial chromosome such as a mammalian artificial chromosome (MAC), a human artificial chromosome (HAC) or comprising an origin of replication and a sequence of nucleotides which:

(i) directs a conformation defining a human neocentromere or a functional derivative thereof or a latent, synthetic or hybrid form thereof wherein said neocentromere is capable of associating with CENP-A and CENP-C or antibodies thereto; and

(ii) contains no substantial α-satellite DNA repeat sequences;

said sequence of nucleotides flanked by eukaryotic (e.g. mammalian) telomeric sequences which are in turn flanked by yeast telomeric sequences wherein a unique enzyme site is located between the human and yeast telomeric nucleotide sequences such that upon contact with said enzyme, the yeast telomeric sequences are removed and the eukaryotic (e.g. mammalian) telomeric sequences are exposed.

Still another aspect of the present invention provides a genetic construct comprising an origin of replication and a first nucleic acid molecule defining a human neocentromere or a functional

derivative thereof or latent, synthetic or hybrid form thereof, a second nucleic acid molecule encoding a peptide, polypeptide or protein, wherein said first and second nucleic acid molecules are flanked by a first set of eukaryotic (e.g. mammalian, such as human) telomeric sequences which are in turn flanked by a second set of eukaryotic (e.g. yeast) telomeric sequences wherein there are unique enzyme sites between the first and second telomeric sequences such that upon contact with a required enzyme, the second telomeric sequences are cleaved off to expose the first telomeric sequences.

BRIEF DESCRIPTION OF THE FIGURES

Figure 1 is a schematic representation showing identification of a YAC contig spanning the marker centromere region. (A) Comparison of GTL banding patterns of mardel 10 and normal chromosome 10. The pair of open arrows indicate the two breakpoints on a normal chromosome 10 in generating the marker chromosome (Voullaire *et al.*, 1993). The long and short arms of the marker chromosome are designated q' and p', respectively, to distinguish them from the q and p arms of the normal chromosome 10. Asterisk denotes the position of a cosmid 10pC38 that was used to "tag" the q'-arm of stretched marker chromosomes in the ANTI-CEN/FISH experiments. (B) A 4-megabase YAC contig (#082) from 10q25.2 region that spans the marker centromere. The tilling path of YACs #0 to #23 and their corresponding CEPH library addresses are shown. (C) FISH mapping of selected YAC clones from contig #082 using normal fluorescence microscopy and standard metaphase chromosomes prepared from transformed lymphoblast cells of patient BE. The distribution of FISH signals (vertical axis) is shown as a percentage of the signals on one arm of the marker chromosome that is in excess of those found on the opposite arm of the chromosome. The total number of fluorescence signals scored for each of the YAC clones is indicated in brackets.

Figure 2 is a photographic representation showing ANTI-CEN/FISH analysis of the marker centromere. (A) Detection of α-satellite DNA using a mixture of α-satellite DNA probes (red signals) under low stringency conditions. Centromeres were counter-labelled with CREST#6 autoimmune antibody (pale blue dots; or white when superimposed on a red background). Chromosomes were prepared from transformed lymphoblast cells of patient BE. The right-hand

panel represents green pseudo-coloring of DAPI images of chromosomes to provide a better definition of chromosome outline. Only the signal for the antibody, but not that for α-satellite, was seen on the marker centromere (arrowed). (B) Simultaneous labelling of stretched human metaphase chromosomes with CREST#6 (red) and anti-CENP-C antibody, Am-C1 (pale blue), with the white color indicating full coincidence of the two antibody signals. (C) Detection of CENP-C on the marker chromosome. Simultaneous labelling of the marker chromosome (arrowhead) with (a) Am-C1 (pale blue) and (b) CREST#6 (red). (c) Combined images of a and b, showing complete coincidence of Am-C1 and CREST#6 signals. (d) FISH analysis of the same cell as a-c using the 10pC38 cosmid probe (pale blue dots and green arrows) to identify the marker chromosome. Some loss of ANTI-CEN signal, especially for the Am-C1 antibody was seen following FISH. (e) Green pseudo-coloring of DAPI images. A colour photograph corresponding to this figure is available upon request.

Figure 3 is a photographic representation showing ANTI-CEN/FISH analysis of cosmid clones on stretched (A, a-f) and superstretched (B) metaphase chromosomes. (a-c) Examples of cosmid signals (white arrows) localized to the q'-region of the marker centromere. (d-f) Examples of cosmid signals (white arrows) localized to the p'-region of the marker centromere. Green arrows indicate positions of the 10pC38 cosmid DNA tag used to mark the q'-end of the marker chromosome. (B) Mapping of Y6C21 onto a superstretched metaphase chromosome. Not included is the 10pC38 q'-tag signal located further to the left of the chromosomal segment shown. ANTI-CEN signals are in red, FISH signals are in pale blue, and overlapping ANTI-CEN and FISH signals are in white. Each of the pictures is accompanied by DAPI images of chromosomes pseudo-coloured in green. A colour photograph corresponding to this figure is available upon request.

Figure 4 Localization of the anti-centromere antibody-binding domain. ***a***, Relative positions of different cosmid and PAC clones within the YAC #082 contig, using YAC-3 as a reference. Cosmids are designated as YnCm, where 'n' denotes the YAC of origin and 'm' denotes the cosmid number. PACs 1-5 are five different PAC clones isolated from a human PAC library (Genome Systems Inc). "HC-contig" represents a group of overlapping cosmids that map tightly around the marker centromere in ANTI-CEN/FISH experiments. A genomic map corresponding

to the depicted YAC region was derived from the DNA of patient BE and shown above the YAC map. S, *Sal*I; K, *Ksp*I; N, *Not*I; Sf, *Sfi*I. ***b***, Cumulative scoring of FISH signals in ANTI-CEN/FISH experiments for cosmids Y3C64, Y6C8, Y3C94, Y7C14, Y4C45, Y6C10, Y6C21, Y3C3, PAC5, Y13C1, Y13C8, and Y17C6. The distribution of FISH signals (vertical axis) is those found on the opposite arm of the chromosome. The total number of fluorescence signals scored for each of the cosmid clones is indicated in brackets. ***c***, Restriction mapping of the 80-kb region covered by the eight overlapping cosmids of the HC-contig. These eight cosmids were derived from four different YACs (YAC-3, YAC-4, YAC-6, and YAC-7) and provided independent confirmation of the map. Furthermore, the map agreed fully with the restriction map of a 120 kb-insert PAC clone (PAC4) that spanned the entire HC-contig region. E, *Eco*RI; R, *Eco*RV; N, *Not*I.

Figure 5 is a representation showing restriction analysis of genomic DNA of patient BE and those of his normal parents using Y6C10 as probe. DNA was resolved on a PFGE (A) or standard agarose gel (B and C). Samples 1, 2 and 3 were fibroblast cultures of mother of BE, father of BE, and patient BE, respectively. Sample 4 was a somatic hybrid cell line BE2C1-18-5F containing the marker chromosome. Fragment sizes are in kilobases.

Figure 6 is a representation of the full nucleotide sequence of the HC-contig DNA derived from normal human chromosome 10q 25.2 region.

Figure 7 is a diagrammatic representation of the method used to retrofit YAC3 and YAC5.

Figures 8A to J are diagrammatic representations of the different vectors used for cloning DNA as YACs by the conventional restriction/ligation methods.

Figures 9 is a diagrammatic representation of circular TAR summarising the recombination process.

Figure 10 is a diagrammatic representation showing modification of TAR vector.

Figure 11 is a diagrammatic representation of the cloning of 10q25 human neocentromere DNA from mardel (10) chromosome. This DNA is designated NC-contig DNA to distinguish it from the HC-contig derived from the corresponding region of the normal chromosome 10. (A) Structural map of the NC-contig region and flanking DNA. Arrows indicate the relative positions and directions of primers used in PCR analyses (Table 3). The restriction sites *EcoR*I, *EcoR*V, *Srf*I, and *Sft*I and *Sft*I are indicated by E, R, Sr and Sf, respectively. The position of the TAR "hook" CE-F2 is represented by the solid box. The hatched bar represents HC- or NC-contig. p′ and q′ refer to the short and long arms of mardel (10), respectively. (B) Circular TAR strategy using the vectors pVC39-Alu/C3-F2(+) and pVC39-Alu/C3-F2(-) for the direct cloning of the neocentromere DNA from mardel (10). The position of the Alu consensus sequence hook is represented by the white box. Crosses denote the sites of recombination between the TAR vector and the genomic DNA at the Alu and C3-F2 hooks during cloning. (C) Structural maps of the resulting circular YACs 5f-52-E8 and 5f-38-F2 containing the neocentromere DNA of the mardel (10) chromosome. The DNA flanking the NC-contig is represented by stippled bars. (D) Structural maps of BAC/E8-1 and BAC/F2-14. Nt represents *Not*I and URA-BAC-neo represents the retrofitting vector BRV1 (Larionov *et al.*, 1997).

Figure 12 is a diagrammatic representation showing specific TAR of HC-region from mardel 10.

The method was as follows: (1) Co-transformation into YPH857; (2) Select HIS^+ colonies; (3) screen for HC-region by PCR; (4) Prepare high-MW DNA; (5) Digest with I-Sce1 to expose hTELS; (6) Transfect HT 1080 cells; (7) Select for $G418^R$; and (8) analyse by PFGE and FISH.

Figure 13 is a diagrammatic representation showing cloning in yeast as YAC/HAC.

Figure 14 is a diagrammatic representation outlining TACT procedure.

Figure 15 is a diagrammatic representation of TACT constructs.

Figure 16A is a representation of the full nucleotide sequence of the NC-contig DNA derived

from mardel (10) and corresponds to the HC-contig DNA region of the normal chromosome 10.

Figure 16B is a representation of the partial nucleotide sequence of the BAC/F2-14 clone that is derived from a region immediately p′ of the NC-contig DNA (see Fig. 11D).

SUMMARY OF SEQ ID NOs.

SEQ ID NO.	DESCRIPTION
1	DNA primer
2	DNA primer
3	Nucleotide sequence of HC-contig
4	Nucleotide sequence of NC-contig
5	BAC-F2 contig 1
6	BAC-F2 contig 2
7	BAC-F2 contig 3
8	BAC-F2 contig 4
9	BAC-F2 contig 5
10	BAC-F2 contig 6
11	BAC-F2 contig 7
12	BAC-F2 contig 8
13	BAC-F2 contig 9
14	BAC-F2 contig 15
15	BAC-F2 contig 33
16	BAC-F2 contig 39
17	BAC-F2 contig 41
18	BAC-F2 contig 42
19	BAC-F2 contig 44
20	BAC-F2 contig 47
21	BAC-F2 contig 47 fragment 1
22	BAC-F2 contig 47 fragment 2
23	BAC-F2 contig 47 fragment 3
24	BAC-F2 contig 47 fragment 4
25	BAC-F2 contig 47 fragment 5
26	BAC-F2 contig 47 fragment 6

27	BAC-F2 contig 47 fragment 7
28	BAC-F2 contig 47 fragment 8
29	BAC-F2 contig 47 fragment 9

ABBREVIATIONS USED IN THE SUBJECT SPECIFICATION

mardel (10):	Marker chromosome from patient BE; comprises a rearrangement of chromosome 10.
HAC:	Human artificial chromosome
YAC:	Yeast artificial chromosome
MAC:	Bacterial artificial chromosome
PLAC:	Plant artificial chromosome
neocentromere:	A centromere containing no substantial α-satellite DNA
CENP:	Centromere binding protein
HC-contig:	Region of normal chromosome 10 comprising neocentromere
E8:	q′ end/region of mardel (10) neocentromere
F2:	p′ end/region of mardel (10) neocentromere
BE:	Patient from which mardel (10) identified
TAR:	Transformation-associated recombinant
PCR:	Polymerase chain reaction
Marker neocentromere:	neocentromere on mardel (10).
NC-contig	region of mardel (10) chromosome comprising neocentromere

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

The present invention is predicated in part on the identification and isolation of nucleic acid molecules exhibiting neocentromeric properties. In accordance with the present invention, a neocentromere is considered a centromere which does not contain substantial α-satellite DNA repeat sequences and, when activated, is capable of functioning as a centromere. The term

"substantial" in this context means that the nucleic acid molecule does not contain detectable α-satellite by FISH analysis under medium stringency conditions. The neocentromere may contain a small number of highly diversed α-satellite DNA. In primates, α-satellite DNA is consider 171bph in length. An nucleic acid molecule containing an activated neocentromere or a neocentromere otherwise functioning as a centromere facilitates in accordance with the present invention, the nucleic acid molecule replicating, remaining extra-chromosomal and segregating with cell division. Reference herein to "neocentromere" is taken to mean a centromere substantially devoid of α-satellite DNA repeat sequences.

Accordingly, one aspect of the present invention provides an isolated nucleic acid molecule comprising a sequence of nucleotides which defines an eukaryotic neocentromere.

More particularly the present invention provides an isolated nucleic acid molecule comprising a sequence of nucleotides derived from a eukaryotic chromosome and encompassing a neocentromere which nucleic acid molecule when introduced into a compatible cell is capable of replicating, acting as an extra-chromosomal element and segregating with cell division.

The present invention is exemplified herein by the identification and cloning of a human neocentromere. This is done, however, with the understanding that the present invention extends to all eukaryotic neocentromeres such as from mammalian, plant, aviary, insect, fungal, yeast and reptilian chromosomes. The most preferred neocentromere, however, is from human chromosomes and their mammalian homologues.

The present invention is predicated in part on the identification of an unusual chromosomal marker in a patient designated "BE". The chromosomal marker is referred to as "mardel (10)" and results from a rearrangement of human chromosome 10. The mardel (10) marker is mitotically stable and, in accordance with the present invention, contains a functional neocentromere at a location regarded as non-centromeric. The neocentromere at mardel (10) is located between q24 and q26 on chromosome 10 and more particularly around q25. Even more particularly, the neocentromere maps to q25.2 on chromosome 10. The present invention is exemplified by DNA cloned from the q24-q26 region of the mardel (10) chromosome as well

as the corresponding region on normal human chromosome 10. These DNA molecules contain a functional neocentromere. The present invention extends, however, to any neocentromere or any chromosome in mammalian and non-mammalian animals as well as plants, yeasts and fungi.

For convenience, the DNA clones from the mardel (10) chromosome as well as from normal human chromosome 10 are summarised in Figure 11. The neocentromere located at or around 10q25 is located on a clone designated the "HC-contig". DNA clones from mardel (10) are referred to as "E8" or the "NC-contig" which extends from the long arm (q′) of mardel (10) towards the short arm (p′). Clone F2 extends further p′ from E8 (see Figure 11). It is emphasised, however, that the present invention extends to any neocentromere on any human chromosome as well as neocentromeres on other mammalian and non-mammalian chromosomes including chromosomes from plants, insects, reptiles, yeast and fungi.

The present invention further contemplates a nucleic acid molecule or its chemical equivalent having a tertiary structure which defines a human neocentromere or a functional derivative thereof or a latent, synthetic or hybrid form thereof or its mammalian or non-mammalian homologue.

Even more particularly, the present invention is directed to an isolated nucleic acid molecule having a sequence of nucleotides or their chemical equivalents which directs a conformation defining a human neocentromere or a functional derivative thereof or a latent, synthetic or hybrid form thereof or its mammalian or non-mammalian homologue wherein the centromere associates with centromere binding proteins (CENP) -A and CENP-C or antibodies thereto.

Reference herein to "latent" in relation to a centromere includes reference to a centromere not normally functional but nevertheless activatable under certain conditions. A latent centromere may also be considered as a neocentromere provided it has no substantial α-satellite DNA repeat sequences.

The size of the neocentromere in accordance with the present invention may range from about

50 bp to about 1500 kbp, from about 70 bp to about 1000 kbp, from about 75bp to about 800 kpb, from about 80 bp to about 500 kbp, from about 85 bp to about 200 kbp, from about 90 bp to about 100 kbp, from about 100 bp to about 1 kbp, about 120 bp to about 500 bp, about 180 bp to about 300 bp. In one particular embodiment, the centromere is approximately 60-100 kbp. In another embodiment, the centromere is about 80 kbp.

The nucleic acid molecule encompassing the HC-contig for human chromosome 10 of the present invention set forth in Figure 6 (SEQ ID NO: 3). The nucleic acid molecule encompassing the NC-contig (part of E8) from mardel (10) is set forth in Figure 16A (SEQ ID NO: 4). The nucleic acid molecule encompassing F2 of mardel (10) is set forth in Figure 16B as separate contigs (SEQ ID NOs: 5-29). The nucleic acid molecules have a tertiary structure and the neocentromere is a conformation of nucleotides within this tertiary structure. Accordingly, the neocentromere is not defined by a linear sequence of nucleotides although this linear sequence directs the conformation which in turn defines the neocentromere. Although this aspect of the present invention is exemplified using the nucleotide sequence set forth in Figure 6, 16A and 16B, the subject invention extends to any sequence directing a conformation defining a centromere and hybridising to the sequence set forth in one or more of Figures 6, 16A and/or 16B under low stringency conditions at 42°C and/or which comprises a nucleotide sequence having at least about 40% nucleotide similarity to one or more sequences set forth in Figures 6, 16A and/or 16B. Preferably, the percentage similarity is at least about 50%, more preferably at least about 60%, still more preferably at least about 70%, even more preferably at least about 80-90% or above such as 95%, 97%, 98% and 99%.

Another embodiment of the present invention is directed to YAC 3 and YAC 5 encompassing the HC contig and flanking sequence as well as nucleotide sequences related to YAC 3 and/or YAC 5 at the homology, similarity or hybridization levels.

Reference herein to a low stringency at 42°C includes and encompasses from at least about 1% v/v to at least about 15% v/v formamide and from at least about 1M to at least about 2M salt for hybridisation, and at least about 1M to at least about 2M salt for washing conditions. Alternative stringency conditions may be applied where necessary, such as medium stringency, which

includes and encompasses from at least about 16% v/v to at least about 30% v/v formamide and from at least about 0.5M to at least about 0.9M salt for hybridisation, and at least about 0.5M to at least about 0.9M salt for washing conditions, or high stringency, which includes and encompasses from at least about 31% v/v to at least about 50% v/v formamide and from at least about 0.01M to at least about 0.15M salt for hybridisation, and at least about 0.01M to at least about 0.15M salt for washing conditions. These stringency conditions may be altered dependent on the source of DNA and other factors.

The term "similarity" as used herein includes exact identity between compared sequences at the nucleotide level. Where there is non-identity at the nucleotide level, "similarity" includes differences between sequences which nevertheless result in conformation defining a functional neocentromere.

The nucleic acid molecule of the present invention may comprise a naturally occurring nucleotide sequence from a healthy human subject or may comprise the nucleotide sequence from a human subject exhibiting one or more chromosomal-dependent conditions such as a subject carrying mardel 10 chromosome or a chromosome conferring an equivalent or similar condition or may carry one or more nucleotide substitutions, deletions and/or additions relative to the naturally or non-naturally occurring sequence. Such modifications are referred to herein as "derivatives" and include mutants, fragments, parts, homologues and analogues of the naturally occurring nucleotide sequence. Preferably, the derivatives of the present invention still define a functional neocentromere.

Reference herein to a "neocentromere" includes reference to a functional neocentromere or a functional derivative thereof meaning that it is capable of facilitating sister chromatid cohesion and chromosomal segregation during mitotic cell divisions and/or is capable of associating with CENP-A and/or CENP-C and/or is capable of interacting with anti-CENP-A antibodies or anti-CENP-C antibodies. Generally, and preferably, the neocentromere is incapable of interacting with CENP-B or anti-CEP-B antibodies. Alternatively, the neocentromere may be a latent centromere capable of activation by epigenetic mechanisms. The neocentromere may also be a hybrid of other human, mammalian, plant or yeast neocentromeres. Synthetic neocentromeres

provided by, for example, polymeric techniques to arrive at the correct confromation are also contemplated by the present invention. All such forms and definitions of neocentromere are encompassed by use of this term.

Another aspect of the present invention provides an isolated nucleic acid molecule or chemical equivalent having the following characteristics:

(i) comprises a nucleotide sequence or chemical equivalent directing a conformation which defines a neocentromere or a functional derivative thereof or a latent, synthetic or hybrid form thereof or;

(ii) comprises a nucleotide sequence or chemical equivalent substantially as set forth in one or more of Figures 6, 16A and/ or 16B or having at least about 40% similarity thereto or capable of hybridising thereto under low stringency conditions at 42°C; and

(iii) comprises a neocentromere capable of associating with CENP-A or CENP-C or antibodies thereto.

Preferably, the neocentromere is incapable of interacting with CENP-B or antibodies thereto.

In a particularly preferred embodiment, the centromere corresponds to a human genomic region which maps between q24 and q26 on chromosome 10, and in particular q25 on chromosome 10.

The nucleic acid molecule or its chemical equivalent of the present invention defining a conformational neocentromere or functional derivative thereof or latent, synthetic or hybrid form thereof is useful *inter alia* for the generation of artificial chromosomes such as human artificial chromosomes (HACs), mammalian artificial chromosomes (MACs), yeast artificial chromosomes (YACs) and plant artificial chromosomes (PLACs). HACs are particularly useful since they are capable of accommodating large amounts of DNA and are capable of propagation in human cells. The HACs are non-viral in origin and, hence, are more suitable for gene therapy by, for example, introducing therapeutic genes. Furthermore, the HACs remain extra-chromosomal and, hence, have no insertional/substitutional mutagenic potential. The essence of a HAC is the presence of a neocentromere or latent, synthetic or hybrid form thereof which enables stable segregation during cell division. The HAC also remains extra-chromosomal and, hence, is more suitable for

gene therapy. Reference to "extra-chromosomal" means that it does not integrate into the main chromosome and, in effect, is episomal.

Accordingly, the present invention provides a genetic construct comprising an origin of replication for a eukaryotic cell and a nucleic acid molecule encompassing a eukaryotic neocentromere or a functional derivative thereof or a latent, synthetic, hybrid form thereof or its mammalian or non-mammalian homologue flanked by telomeric nucleotide sequences functional in the cell in which the genetic construct is to replicate and wherein said genetic construct when introduced into a cell is a replicating, extra-chromosomal element which segregates with cell division.

More particularly, the present invention further contemplates a genetic construct in the form of an artificial chromosome comprising an origin of replication for a mammalian, human, plant or yeast cell and a nucleic acid molecule encompassing a human neocentromere or a functional derivative thereof or a latent, synthetic or hybrid form thereof or its mammalian or non-mammalian homologue flanked by telomeric nucleotide sequences functional in the cell in which the artificial chromosome is to replicate.

Another embodiment provides a genetic construct in the form of an artificial chromosome comprising an origin of replication for a mammalian, human, plant or yeast cell and a nucleic acid molecule having a tertiary structure which defines a human neocentromere or a functional derivative thereof or a latent, synthetic or hybrid form thereof or its mammalian homologue flanked by telomeric sequences functional in the cell in which the artificial chromosome is to replicate.

Yet another embodiment is directed to a genetic construct in the form of an artificial chromosome comprising an origin of replication for a mammalian, human, plant or yeast cell and a nucleic acid molecule having a sequence of nucleotides which directs a conformation defining a human neocentromere wherein the centromere associates with CENP-A and/or CENP-C or antibodies thereto and does not contain substantial α-satellite DNA repeat sequences, said nucleic acid molecule flanked by telomeric nucleotide sequences functional in the cell which the

artificial chromosome is to replicate.

Still yet another aspect of the present invention relates to a genetic construct in the form of an artificial chromosome comprising an origin of replication for a mammalian, human, plant or yeast cell and a nucleic acid molecule comprising a sequence of nucleotides which:

(i) directs a conformation which defines a neocentromere or a functional form thereof or a latent, synthetic or hybrid form thereof;

(ii) comprises a nucleotide sequence substantially as set forth in one or more of Figures 6, 16A and/or 16B or having at least about 40% similarity to the nucleotide sequences set forth in Figures 6, 16A and/or 16B or is capable of hybridising to one or more of these sequences under low stringency conditions at 42°C;

wherein the neocentromere is capable of associating with CENP-A and/or CENP-C or antibodies thereto and wherein said nucleic acid molecule is flanked by telomeric nucleotide sequences functional in the cell in which the artificial chromosome replicates.

In a preferred embodiment, the genetic construct is a HAC and comprises human telomeric sequences. In a particularly preferred embodiment, the HAC further comprises yeast artificial chromosome (YAC) arms and, hence, becomes a HAC/YAC shuttle vector capable of propagation in human and yeast cells. Preferably, the HAC/YAC contains a unique enzyme site between yeast telomeric sequences and human telomeric sequences such that upon contact with the particular enzyme, the yeast telomeric sequences are removed leaving the human telomeric sequences. Preferably, the unique enzyme site is a yeast specific enzyme site such as I-SceI.

According to this embodiment, there is provided a genetic construct defining a HAC/YAC comprising an origin of replication and a nucleic acid molecule encompassing a human neocentromere or a functional derivative thereof or a latent, synthetic or hybrid form thereof or a mammalian or non-mammalian homologue thereof, said nucleic acid molecule flanked by human telomeric sequences which are in turn flanked by yeast telomeric sequences wherein a unique enzyme site is located between the human and yeast telomeric nucleotide sequences such that upon contact with the enzyme, the yeast telomeric sequences are removed and the human telomeric sequences are exposed.

More particularly, the present invention is directed to a genetic construct defining a HAC/YAC comprising an origin of replication and a nucleic acid molecule encompassing a human centromere or a functional derivative thereof or a latent, synthetic or hybrid form thereof or a mammalian or non-mammalian homologue thereof wherein the neocentromere associates with CENP-A and/or -C or antibodies thereto and does not contain substantial α-satellite DNA sequences wherein said nucleic acid molecule is flanked by human telomeric sequences which are in turn flanked by yeast telomeric sequences wherein a unique enzyme site is located between the human and yeast telomeric nucleotide sequences such that upon contact with said enzyme, the yeast telomeric sequences are removed and the human telomeric sequences are exposed.

Even more particularly, the present invention is directed to a genetic construct in the form of a HAC/YAC comprising an origin of replication and a sequence of nucleotides which directs a conformation defining a human neocentromere or a functional derivative thereof or a latent, synthetic or hybrid form thereof or a mammalian or non-mammalian homologue thereof wherein said neocentromere is capable of associating with CENP-A and/or CENP-C or antibodies thereto, said sequence of nucleotides flanked by human telomeric sequences which are in turn flanked by yeast telomeric sequences wherein a unique enzyme site is located between the human and yeast telomeric nucleotide sequences such that upon contact with said enzyme, the yeast telomeric sequences are removed and the human telomeric sequences are exposed.

Preferably, the length of the nucleotide sequence is between about 30 kpb and 1500 kpb, and more preferably between 60 kbp and 1000 kpb.

In a particularly preferred embodiment, the unique enzyme site is a yeast specific enzyme site such as I-SceI.

The present invention extends to yeast cells and human cells carrying the genetic constructs of the present invention and to proteins produced therefrom.

The genetic constructs may also comprise marker genes and other unique restriction sites to facilitate insertion of adventitious DNA. Accordingly, the genetic constructs of the present

invention may further comprise adventitious or heterologous DNA encoding a product of interest. Preferred products of interest include pharmaceutically useful genes such as genes encoding cytokines, receptors, growth regulators and the like. Endogenous genes may also be replaced by wild-type genes or modified genes.

The adventitious or heterologous DNA may also encode a molecule not synthesised in a sufficient amount in a particular subject and hence the increased copy number permits greater amounts of the molecule being synthesised.

Accordingly, the present invention contemplates a genetic construct comprising an origin of replication and a first nucleic acid molecule defining a human neocentromere or a functional derivative thereof or latent, synthetic or hybrid form thereof or a mammalian or non-mammalian homologue, a second nucleic acid molecule encoding a peptide, polypeptide or protein, wherein said first and second nucleic acid molecules are flanked by a first set of human telomeric sequences which are in turn flanked by a second set of yeast telomeric sequences wherein there are unique enzyme sites between the human and yeast telomeric sequences such that upon contact with said enzyme, the yeast telomeric sequences are cleaved off to expose the human telomeric sequences.

Reference herein to segregate preferably means mitotically stable segregation. Conveniently, stable segregation may be determined as the presence of an artificial chromosome in 40-60% of daughter cells after 4-6 months of continuous passage.

The present invention extends to other artificial chromosome analogues to the HACs and HAC/YACs described above such as MACs and PLACs.

Another aspect of the present invention relates to peptides, polypeptides and proteins which bind, interact or otherwise associate with the human neocentromere of the present invention or its mammalian and non-mammalian homologue. Preferably, the molecules are proteins, referred to as primary (1°) proteins. The 1° proteins bind to the neocentromere and secondary (2°) proteins bind to the 1° proteins before or after association with the neocentromere. The identification

of the human neocentromere in accordance with the present invention provides a mechanism for assaying 1° proteins and 2° proteins which may be important for screening chromosomes in, for example, genetic disorders. This is particularly the use in Down's Syndrome which results from defective chromosome segregation.

The 1° proteins are readily detected by, for example, a gel shift assay. The nucleic acid molecule of the present invention defining the human neocentromere is digested, labelled and contacted with nuclear extract putatively containing the 1° proteins and resolved on a gel. When a 1° protein binds to a fragment carrying a binding portion of the neocentromere, the DNA fragment migrates in the gel at a slower rate due to the bound protein.

The present invention extends to purified 1° proteins capable of association with the subject centromere and to genetic sequences encoding same and to antibodies thereto.

The neocentromeres of the present invention are readily identified and characterised using, for example, human fibrosarcoma cell lines. For example, DNA suspect of carrying a neocentromere, is introduced into fibrosarcoma cells in a linear form, generally together with a telomeric sequence. The cells are then screened for the presence of replicating, extra-chromosomal and segregating elements, referred to as mini chromosomes.

The present invention further encompasses eukaryotic cells carrying replicating, extrachromosomal and segregation nucleic acid molecules. Preferably the eukaryotic cells are mammalian cells and most preferably human cells. The nucleic acid molecules according to this aspect of the present invention are preferably as herein described. Particularly preferred cells are HT-38, HT-47, HT-54, HT-190, HT-191, BAC/E8-1, and BAC/F2-14.

The present invention is further described by the following non-limiting Figures and Examples.

EXAMPLE 1

YAC and Cosmid Probes for FISH

YACs carrying specific STSs were identified (Moir *et al.*, 1994) by PCR-based screening of YAC libraries prepared in pYAC4 vector at the Center for Genetics in Medicine at Washington University (Brownstein *et al.*, 1989) and at the CEPH (Albertsen *et al.*, 1990). Cosmid DNA inserts (35-40 kb) were ligated to SuperCos I vector (Stratagene) and packaged with Gigapack III Gold extract (Stratagene) according to the manufacturer's instructions. YAC probes were prepared by Alu-PCR of total yeast genomic DNA using primers 5'-GGATTACAGG(C/T)(A/G)TGAGCCA-3' [SEQ ID NO:1] and 5'-(A/G)CCA(C/T)TGCACTGCAGCCTG-3' [SEQ ID NO:2] according to published method (Archidiacono *et al.*, 1994). For probe labelling, 1 μg of the YAC PCR products or whole cosmid DNA isolated by CsCl centrifugation or Qiagen column was used. The DNA was labelled with Biotin-16-dUTP (Boehringer Mannheim) using a NICK translation kit (Boehinger Mannheim). A probe mix of 6-10 μg/ml of biotinylated probe DNA, 300 μg/ml of COT-1 DNA (Boehringer Mannheim), 500 μg/ml of carrier salmon sperm DNA and, where indicated, 10 μg/ml of biotinylated 10pC38 tag DNA was ethanol precipitated, resuspended in a hybridization mix of 50% v/v formamide in 2 x SSC and 10% w/v dextran sulphate, denatured at 95°C for 5 min, preannealed for 30-60 min at 37°C to suppress repetitive sequences, before adding to slides. FISH of α-satellite and satellite III probes was performed under low stringency as previously described (Voullaire *et al.*, 1993).

EXAMPLE 2

Somatic Cell Hybrids and Other Cell Lines

Skin fibroblasts and transformed lymphoblast cell lines were established from patient BE (Voullaire *et al.*, 1993) and from his normal parents. The presence of the mardel 10 chromosome in the patient cell lines was confirmed by FISH. In addition to these cell lines, two somatic cell hybrids were produced by fusing cultured fibroblast cells derived from patient BE with the Chinese hamster ovary cell line CHO-K1 using polyethylene glycol. Hybrid cells were selected in a proline-free medium for the glutamic oxaloacetic transaminase-1 (GOT-1) gene located in

10q24-q25 region. One of the hybrid cell lines, designated BE2C1-18-1f, was shown to contain the normal chromosome 10 but not the marker chromosome, while another hybrid cell line, designated BE2C1-18-5F, contained the marker chromosome but not the normal chromosome 10 of patient BE. The presence or absence of these chromosomes was established by karyotyping and ANTI-CEN/FISH probing. In addition, PCR analysis of an STS (sequence tagged site) marker, AFM259xg5, which resided on YAC-3, confirmed the status of these chromosomes in the hybrids and excluded the presence of submicroscopic fragments of the marker centromere region within the genome of BE2C1-18-1f, or the presence of the corresponding region of normal chromosome 10 within the genome of BE2C1-18-5f. Use of this STS marker also demonstrated that the mardel 10 chromosome has originated from the patient's father.

EXAMPLE 3

Antisera

Antiserum CREST #6 was from a patient with calcinosis, Raynaud's phenomenon, esophageal dysmotility, sclerodactyly and telangiectasia (a constellation of symptoms commonly referred to as "CREST"; Moroi *et al.*, 1981; Fritzler and Kinsella, 1980; Brenner *et al.*, 1981). Western blot analysis of this antiserum indicated that the primary antigens detected were human CENP-A and CENP-B. A specific anti-CENP-C polyclonal antibody, designated Am-C1, was produced by the inventors by expressing a partial mouse CENP-C polypeptide (amino acid #41 to 345) as a GST-fusion product in *E. coli*, followed by gel purification of the product and its use as an antigen for antibody production in rabbit.

EXAMPLE 4

Preparation of Standard Metaphase Chromosomes for FISH analysis

Actively replicating transformed lymphoblasts were incubated at 37°C for 17 h in the presence of 0.1M final concentration of thymidine before they were centrifuged at 2000 rpm for 10 min, washed with pre-warmed RPMI, and incubated for a further 5-6 h. 15 min before harvesting, colcemid (10μg/ml) was added. Cells were harvested according to standard cytogenetic techniques using 0.075M KCl hypotonic solution for 15 min at 37°C, followed by three fixative

washes in ice cold methanol/acetic acid 3:1, dropped onto clean glass slides, and stored dessicated at -20°C until required.

EXAMPLE 5

Preparation of Mechanically Stretched Chromosomes for ANTI-CEN/FISH Mapping

METHOD - I

This is an adaptation of the method described by Page *et al.* (1995). Colcemid (10μg/ml) was added to actively dividing transformed lymphoblasts for 2-3 h, before the cells were centrifuged at 1500 rpm for 10 min, washed in PBS, and resuspended in 0.075M KCl hypotonic solution for 10 min at RT at a concentration of approximately 5 x 10^4 cells/ml; the use of fewer cells here gave better stretching of the chromosomes. 200-300µl of this suspension were then cytocentrifuged onto clean microscope slides using a Cytospin 2 (Shandon) at 1000 rpm for 5 min at high acceleration. The slides were immediately removed, placed flat in a shallow dish and very gently flooded with KCM (Potassium Chromosome Medium: 120 mM KCl, 20mM Nacl, 10mM Tris-HCl, 0.5mM Na_2EDTA, 0.1% v/v Triton X-100) (Jeppesen *et al.*, 1992). After 10 min at RT, immunofluorescence was performed without fixation (Earnshaw and Migeon, 1985; Earnshaw *et al.*, 1989; Jeppesen *et al.*, 1992; Jeppesen and Turner, 1993). KCM buffer was gently aspirated and 50µl of CREST#6 serum [diluted 1:50 in 1 x TEEN (1mM Triethanolamine HCl, 0.2 mM Na_2EDTA, 25 mM NaCl), 0.1% v/v Triton X-100, 0.1% w/v BSA] was added to the cell area of the slide and covered with a parafilm coverslip. The slides were incubated for 30 min at 37°C, then washed very gently by flooding in 1 x KB^- [10 mM Tris-HCl (pH7.7), 0.15M NaCl, 0.1% w/v BSA), three rinses of 3 min each at RT. The primary antibody was detected with Texas Red-conjugated Affini-pure Rabbit anti-Human IgG (H&L) (Jackson Laboratories) diluted 1:50 in 1 x KB^-. 50 µl was added to each slide, covered with a parafilm coverslip, and incubated for 30 min at 37°C. The slides were again gently washed by flooding in 1 x KB^- for 2 min at RT, before they were fixed by flooding in 10% v/v formalin in KCM for 10 min at RT, followed by three rinses of 3 min each in distilled water. If FISH was not performed the slides were rinsed in PBS and mounted in DAP1 (0.25 µg/ml) in DABCO antifade mountant. [In experiments where CREST#6 and Am-C1 antisera were simultaneously used to label the centromere (Figs. 2B and C), the above procedure was

followed except for the addition of Am-C1 diluted 1:100 together with CREST#6, and the Am-C1 antibody was detected using 1:100 diluted Donkey anti-Rabbit DTAF (Jackson Laboratories)].

If FISH was to be performed on the slides, they were then given a second fix in 3:1 methanol/acetic acid for 15 min at RT. The slides were air dried for at least 5 min and either processed for FISH or stored at -20°C for up to several days before continuing. For FISH, the slides were dehydrated at RT in 70%, 90%, 100% v/v ethanol (2 min each) and air dried. Chromosomal DNA was denaturated in deionised 70% v/v formamide/2xSSC, pH 7.0 at 82°C for 8 min followed by immediate dehydration in 70%, 90% and 100% v/v ethanol at -20°C for 2 min each, then air dried for at least 10 min. (This high temperature of denaturation was critical to obtain maximum FISH signals). An amount of 15 µl of the prepared probe was added to each slide, covered with a $22mm^2$ coverslip, and sealed with rubber cement. Slides were hybridized overnight in a humid chamber at 37°C, then rinsed in 2 x SSC at RT, followed by 3 washes of 0.1 x SSC at 60°C for 5 min each, rinsed again in 2 x SSC, and immersed in a blocking agent of 5% non fat milk in 4 x SSC for 10 min at RT. Probe hybridization was detected by incubation with FITC-conjugated avidin at 37°C for 30 min, followed by three washes of 5 min each at RT in wash buffer (4 x SSC, 0.05% v/v Tween-20). Signals were amplified by incubating with goat anti-avidin D antibodies for 30 min at 37°C, followed by three washes of 5 min each at RT in wash buffer, then with another layer of avidin-FITC for 30 min at 37°C, before the slides were washed in wash buffer, rinsed in PBS, and counter-stained with DAP1 (0.25 µg/ml) in DABCO mountant.

METHOD - II

The following method was modified from that of Haaf and Ward, (1994). Actively dividing lymphoblast cells were treated with 10µg/ml colcemid for 2-3h, washed in PBS and resuspended in a hypotonic solution consisting of 10mM Hepes (pH7.3), 30mM glycerol, 1.0mM $CaCl_2$ and 0.8mM $MgCl_2$, at a cell density of approx. 2.5 x 10^2/ml. After 10 min of hypotonic treatment at RT, 300 µl were cytocentrifuged (Shandon - Cytospin 2) onto glass slides at 800 rpm for 4 min. The slides were immediately removed from the centrifuge, dried

for 15 sec, fixed in methanol at -20°C for 20-30 min, rinsed in acetone at -20°C for a few sec, then washed in 3 rinses of PBS at RT. Immunofluorescence staining was done using CREST#6 at a dilution of 1:50 in PBS. After incubation at 37°C for 30 min, the slides were washed three times in PBS for 2 min each. This primary antibody was then detected by a further incubation for 30 min at 37°C with Texas Red-conjugated Rabbit anti-Human IgG diluted at 1:50 in PBS. The slides were fixed in 10% v/v formalin in KCM for 10 min at RT, then washed in 3 rinses of distilled water and drained. Before FISH was performed, slides were fixed in methanol/acetic acid 3:1 for 15 min at RT and air dried. Chromosomal DNA was denatured in 70% v/v deionised formamide (pH7.0) in 2 x SSC at 82°C for 4-6 min. After dehydration in an ice cold ethanol series the slides were air dried, and used for FISH as described for Method I. Slides could be stored covered in foil at RT after methanol/acetic acid fix for up to several weeks before FISH.

Both methods I and II were used to obtain the results shown in Figs. 2B, 2C, 3 and 4B.

EXAMPLE 6

Image Analysis

Hybridization signals for YAC mapping on standard metaphase preparations utilized a normal fluorescence microscope. Images for the ANTI-CEN/FISH experiments were analyzed on a Zeiss Axiolab fluorescence microscope equipped with a 100x objective and a cooled CCD camera (Photometrics Image Point) controlled by a Power Mac computer. Gray scale images were captured separately using a LUDL filter wheel and controller for Texas Red, FITC and DAPI. These images were pseudocoloured and merged using IPlab Spectrum software from Signal Analytics Corporation. A number of difficulties were commonly associated with the ANTI-CEN/FISH technique: (a) the deliberate "stretching" of the chromosomes, whilst increasing the resolution of mapping, sometimes caused serious distortion to the chromosomes, often making them quite dysmorphic; (b) FISH treatment following the ANTI-CEN-labelling often significantly reduced the ANTI-CEN signals; (c) more highly stretched chromosomes (which would potentially give better mapping resolution) generally gave weaker ANTI-CEN signals; and (d) the ANTI-CEN signal on the mardel 10 centromere was usually weaker than

those of the other human chromosomes. Thus, a cell would only be considered informative and used for scoring if both the p'- and q'-arms of the mardel 10 chromosome were discernible and separated by a discrete ANTI-CEN signal. In addition, FISH signals for both the test probe and the 10pC38 cosmid tag (used to identify the q'-arm of, and thus orientate, the marker chromosome) must be clearly present. Using these criteria, the overall frequency of informative cells was found to be approximately 1 in every 20-30 metaphases analyzed.

EXAMPLE 7

Restriction Analysis of Patient DNA

High-molecular weight genomic DNA was extracted from cultured fibroblast cell lines of patient BE and those of his parents and digested with different enzymes to generate restriction fragments ranging from <1kb up to ~1 Mb. The digested DNA was resolved either on a standard agarose gel or by pulsed-field gel electrophoresis (PFGE) using a Bio-Rad CHEF-XA Mapper. For filter hybridization, 50-100 ng of whole cosmid or PAC DNA was labelled by random priming. The labelled probe was then added to 2 ml of hybridization buffer (0.5M Na_2HPO_4, 7% w/v SDS, 1% w/v BSA, 1mM EDTA, pH. 7.0) containing 500 μg of human placental DNA (Sigma). The mixture was boiled for 5 min, then placed in a 65°C water bath for preannealing of repetitive DNA for 90 min. The preannealed probe mix was then added to prehybridizing filters and hybridized overnight at 65°C. Post-hybridization washes were at a final stringency of 0.1 x SSC, 0.1% w/v SDS at 68°C.

EXAMPLE 8

Identification of a YAC region spanning the marker centromere

The initial search for DNA sequences spanning the centromere of the mardel 10 chromosome was based on fluorescence in situ hybridization (FISH) of existing cosmid and YAC clones (Moir *et al.*, 1994; Zheng *et al.*, 1994) that have been mapped to the q24 - q26 region of the normal human chromosome 10 where the new marker centromere was formed (Voullaire *et al.*, 1993) (Fig. 1A). This search led to the identification of a 4 megabase YAC contig (designated #082) that spanned the marker centromere region (Fig 1B). Fig. 1C graphically presents the

FISH mapping results with selected YACs from this contig. As can be seen, two of the YACs (YACs-1 and YAC-2) mapped to the q'-side of the marker centromere, whereas the remaining YACs mapped to the p'-side of the centromere. The low signal level observed for YAC-3 was due to a large proportion of this probe hybridising directly on the centromere itself. These results, therefore, provided evidence that YAC contig #082 spanned the marker centromere, and that the centromere region was likely to be within YAC-3, where the "cross-over" between the q' and p' signals occurred.

EXAMPLE 9

Development of Improved ANTI-CEN/FISH Methods for the Simultaneous Detection of Marker Centromere and Single-copy Cosmid DNA Probes

Although normal fluorescence microscopy and FISH analysis of standard metaphase chromosomes were adequate for the initial identification of the YAC contig spanning the marker centromere, methods with significantly higher sensitivity and resolution were needed to allow further walking into the marker centromere DNA. Three requirements have to be satisfied by these methods: (a) the metaphase chromosomes have to be extended to offer much greater mapping resolution, (b) the centromeres have to be more precisely defined than that offered by a cytogenetic constriction, and (c) the methods should allow simultaneous visualization of both the centromere antibody and FISH signal. Two published methods were explored (designated here as ANTI-CEN/FISH methods) based on extending metaphase chromosomes by mechanical stretching and labelling of the neocentromere by autoimmune antibodies (Haaf and Ward, 1994; Page *et al.*, 1995). Since these methods were originally established for the labelling of normal centromeres and for FISH analysis of highly repeated DNA, they were modified (see Example 4) to allow detection of the generally reduced ANTI-CEN signal of the subject marker neocentromere and the lower FISH signals resulting from the use of single-copy cosmid DNA probes.

With the improved detection methods, the status of α-satellite and satellite III DNA on the marker neocentromere was reassessed, since this was previously determined using standard

microscopy and FISH (Voullaire *et al.*, 1993). Fig. 2A shows the result of antibody labelling using CREST#6 and FISH using α-satellite DNA, and indicated the absence of detectable signal on the marker centromere. The same result was obtained when the experiments were repeated without ANTI-CEN-labelling, ruling out the possibility that the anti-centromere antibody might have obscured any weak FISH signals. Similar results were obtained with satellite III DNA. Since in separate reconstruction experiments, it was possible to demonstrate the sensitivity of the procedure in detecting a single-copy DNA probe of less than 1.5 kb, and making the reasonable assumption that the low-stringency hybridization conditions used for the α-satellite and satellite III DNA which, by virtue of the use of >100-fold excess of probes and the strong hybridisation of these probes to all the other centromeres, would have allowed the detection of any related sequences, it can be concluded that these satellite are absent.

EXAMPLE 10

Co-localization of CENP-C and CENP-A on the Marker neocentromere

To test if CENP-C is present on the marker centromere, a specific rabbit polyclonal antibody was prepared against a recombinant product of mouse CENP-C. This antibody, designated Am-C1, reacted strongly with the centromeres of rodent and human chromosomes. Fig. 2B shows results for the labelling of stretched human metaphase chromosomes using this antibody simultaneously with the CREST#6 autoimmune antibody. As can be seen, irrespective of the degree of chromosome stretching, the signals for the two antibodies coincided fully on all the centromeres. The localization of these two antibodies on the marker chromosome was further determined by employing the 10pC38 cosmid tag in an ANTI-CEN/FISH experiment to identify the marker chromosome. The results indicated that both the antibody signals were clearly present and again coincided completely on the marker centromere (Fig. 2C, a-e). Although CREST #6 was known to bind CENP-A and CENP-B, indirect evidence suggests that binding to the marker centromere presumably occurred *via* CENP-A since the presence of the marker centromere was previously demonstrated not to bind CENP-B (Voullaire *et al.*, 1993). The above results, therefore, established the localization of CENP-C, and probably CENP-A, on the marker centromere.

EXAMPLE 11

Localization of the anti-centromere antibody-binding domain

For further walking into the marker centromere region, cosmid libraries were prepared from total yeast genomic DNA containing YACs-2, -3, -4, -6, -7, -13, and -17. Cosmid clones containing human DNA inserts were isolated by hybridization with human COT-1 DNA using low stringency. All resulting cosmids were screened by standard FISH to confirm their localization to the expected marker centromere and normal chromosome 10 regions, and to eliminate clones that might have originated from other genomic sites due to chimeric YACs. Positive clones were then analyzed further with the ANTI-CEN/FISH methods, using CREST#6 to label the centromere. Fig. 3*a* (I and II) show examples of cosmid signals that mapped to the q'- and p'-side, respectively, of the marker centromere in the ANTI-CEN/FISH experiments. The cosmid tag (clone 10pC38) was used in these experiments to define the q' arm of the marker chromosome. For cosmid walking, we concentrated on clones derived from YAC-3 since FISH mapping of YAC contig #082 indicated that the marker centromere region was likely to be within this YAC. Fig. 4*a* shows a restriction map of the region covered by this and surrounding YACs and compares this map with a genomic map derived from patient BE. The relative positions of a series of cosmid clones (including five independent PACs) were also determined and placed on the YAC map. Fig. 4*b* presents the ANTI-CEN/FISH results obtained with a number of the cosmid clones and one of the PAC clones. Clones Y3C64, Y6C8, and Y3C94 localized preferentially to the q'-side, while Y13C1+C8 and Y17C6 localized preferentially to the p'-side of the marker centromere, suggesting that the nucleus of the antibody-binding domain is situated between these two cosmid clusters. Within this central region, a group of cosmid clones comprising the HC-contig (Fig. 4*a*) was found to map closely around the ANTI-CEN signal. Fig. 4*c* shows a restriction map for eight different overlapping clones from this HC-contig. The chromosomal positions of five of these overlapping clones were analyzed in detail using ANTI-CEN/FISH. Fig. 4*b* shows the cumulative results for more than 60 informative chromosomes for each of these five probes. The results indicated that Y7C14 mapped preferentially q'- of the antibody-binding domain, while the remaining four clones (Y4C45, Y6C10, Y6C21 and Y3C3) mapped preferentially to the p'-side. In addition, the results for PAC5 (a 75 kb-insert PAC clone that overlapped with the p'-end of PAC4 by approximately 5 kb; see Fig. 4*a*) provided further

evidence for the emergence of the HC-contig region onto the p'-arm. Based on these results, we conclude that the eight contiguous cosmid clones within the HC-contig shown in Fig. 4*c*, which together constitute ~80 kbp of DNA, have defined the nucleus of the antibody-binding domain of the marker centromere.

From the above ANTI-CEN/FISH results, it was difficult to determine if the sequences of the HC-contig and its surrounding DNA, both originally derived from a normal individual, were part of the marker centromere DNA, or whether these sequences simply flanked a transposed centromere DNA with an unrelated nucleotide composition. However, supporting evidence from the ANTI-CEN/FISH experiments suggested that the DNA of the HC-contig region appeared to be a part of the marker centromere. This came from the mapping of Y6C10 and Y6C21 onto superstretched chromosomes that were occasionally detected in the slide preparations. An example of such mapping is shown in Fig. 3*b* using Y6C21. As can be seen, whilst a significant portion of Y6C21 hybridized to the p'-side of the CREST signal on the highly extended chromosome, a substantial portion of the cosmid DNA also overlapped directly with the CREST signal. This suggests that at least part of the HC-contig region actually comprises the same DNA sequence as the marker centromere. This possibility was further investigated by detailed genomic mapping.

EXAMPLE 12

The Marker Centromere DNA has a Similar or Identical Sequence Organization as the HC-Contig

The genomic organization of the HC-contig region was compared with that of the corresponding DNA region of the mardel (10) chromosome. Three overlapping cosmids (Y7C14, Y6C10, and Y4C7, the latter being essentially the same as Y6C21; Fig. 4C) from the HC-contig were used as probes to analyze the restriction patterns of genomic DNA prepared from patient BE and those of his karyotypically normal parents. Fig. 5 shows examples of the band patterns obtained with Y6C10, while Table 1 summarizes the results for all the enzymes tested with Y7C14, Y6C10 and Y4C7. The detection of a single band on PFGE gels with a number of the enzymes indicated that the cosmid DNA sequences were unique within the

human genome (*Sfi*I, *Sal*I, *Ksp*I, *Kpn*I and *Bcl*I in Fig. 5A; Table 1). The detection of a single on PFGE gels with a number of the enzymes (*Cla*I in Fig. 5A; Table 1) could be explained by differential methylation of different restriction sites found in this region (Nelson and McClelland, 1991); the reproducibility of these multiple band patterns ruled out incomplete digestion as a possible cause. The multiple bands detected with the more frequent cutting enzymes on a standard gel (Fig. 5B and Table 1) were a result of the presence of cleavage sites present within the probe DNA, since similarly digested cosmid DNA electrophoresed next to the genomic DNA yielded identical patterns for all the bands not containing cosmid vector sequences. In all, 37 enzymes were used to generate more than 160 different fragments for the three cosmid probes (Table 1). The results indicated that, except for a polymorphic fragment found in one of the parents, an identical banding pattern was present in the genomic DNA of patient BE and those of his parents. Furthermore, when the restriction patterns obtained for the genomic DNA of patient BE were compared with those of the smatic hybrid cell line BE2C1-18-5F, which contained the marker chromosome but not the normal chromosome 10, no detectable difference was seen between the two DNA preparations within the HC-contig region (Fig. 5C).

In addition to Y7C14, Y6C10 and Y4C7, a host of other probes from within or surrounding the HC-contig have been tested, each with an average of 12 different informative enzymes. These probes included PAC4 (which spanned the entire HC-contig region shown in Fig. 4C), Y3C64, Y3C109, Y6C6, Y6C8, Y3C94, PAC1, Y3C90, Y4C4, Y4C8, Y4C13, and Y3C33. The results again indicated identical restriction enzyme patterns between patient BE and normal DNA. Thus, through the analysis of a relatively large number of probes covering about 500 kb of YAC-3 around the HC-contig region, and the use of a high density of restriction enzymes that generated a range of fragments from <1 kb to ~1 Mb, it was evident that the marker centromere DNA and a substantial stretch of its adjoining regions showed no detectable difference against the corresponding genomic region of the normal chromosome 10.

Since a potential limitation of the above Southern blot analyses was that highly repeated sequences were not detected because of the preannealing step used in the hybridisation procedure, a different approach was employed to compare the DNA of the marker chromosome

and that of the normal chromosome 10. In this approach, oligonucleotide primers from different regions of the HC-contig were used to prepare a series of PCR fragments from the BE2C1-18-5F and BE2C1-18-1F hybrid cell lines. Electrophoretic comparison of such fragments, which randomly covered approximately 40 kb of the HC-contig, indicated no detectable difference between the two chromosomes and provided independent support for the results obtained in the Southern blot analyses. Thus, it can be concluded that the sequence organization of the marker centromere region is similar, if not identical, to that found in the HC-contig region of the normal chromosome 10.

EXAMPLE 13

Implications for Centromere Study and Mammalian Artificial Chromosome Construction

The mammalian centromere has been difficult to study due to the massive amount of repetitive DNA normally associated with it. By avoiding such repetitive DNA and analyzing the unusual centromere found in the present marker chromosome, the inventors have created a much more tractable system for centromere studies. The present analysis has already shed some light on the important question of DNA sequence versus conformational requirement of a centromere, and on the intriguing concepts of latent centromeres and epigenetic mechanisms. One urgent application of this DNA is to use it to identify the primary protein(s) which binds to the centromeric DNA. Another important application of the marker centromere DNA is in the construction of mammalian artificial chromosomes. Such artificial chromosomes offer a potentially powerful vehicle for the structural and functional analysis of chromosomes, for the genetic manipulation of plants and animals, and for the stable transmission of therapeutic genes in human gene therapy. The artificial chromosomes require a functional mammalian centromere, and the marker centromere DNA element of the present invention now provides a suitable centromere especially because of its relatively small size in the absence of α-satellite DNA and its cloning stability, as indicated by the cosmid, YAK and BAC clones of the HC-contig and NC-contig.

EXAMPLE 14

Sequence analysis

Figures 6, 16A and 16B show partial nucleotide sequences for the HC-contig (SEQ ID NO: 3) NC-contig [SEQ ID NO: 4] and F2 (BAC/F2-14) [SEQ ID NO: 5-29] regions, respectively.

EXAMPLE 15

Human Artificial Chromosome (HAC)

The following are examples of the different approaches being used in the inventors' laboratory for the production of a HAC:

Retrofitting of HC-contig DNA from normal chromosome 10

This procedure aims to produce HACs of 100 kb to >1Mb using the region of the normal chromosome 10 containing and surrounding the HC-contig DNA. The generation of a HAC by this approach will provide crucial proof that this normal DNA region can be reactivated to form a functional centromere.

A retrofitting procedure suitable for introducing human telomeres to both ends of any YAC prepared in the pYAC4 vector in the yeast host strain AB1380 has been previously described (Larin *et al.*, 1994; Taylor *et al.*, 1994, 1996). YACs (in particular YAC-3 and YAC-5) spanning the normal HC-contig region are used for retrofitting by plasmid constructs designed to recombine with their pYAC4 vector arms (Figure 7). The construct pLGTEL 1 is used to target the left arms of the YACs. This serves to add a LYS2 yeast selectable marker, gpt element for ultimate selection in mammalian and avian cell culture, and a human telomere. The right arm of the YACs are targeted by homologous recombination with pRANT 11 to produce a final construct where additional markers are introduced along with a second human telomere to cap the construct. Specifically, an ADE2 yeast marker is added and the URA3 gene of the YAC is disrupted, serving a useful role in negative selection of the construct. A neomycin (neo) resistance gene shown to function in mammalian and avian cells is also introduced. The finished

constructs are transfected into different cultured cell lines, including HT1080 (of human sarcoma origin) (Larin *et al.*, 1994; Rasheed *et al.*, 1974), DT40 (a recombination-proficient chicken cell line) (Dieken *et al.*, 1996), and BE2CI-18-5f (a human/hamster somatic hybrid cell line containing the mardel (10) chromosome but not the normal chromosome 10).

In vitro cloning of HC-region into YAC/HAC vectors

The different vectors used for the cloning of the normal and mardel (10) centromeric DNA in the preparation of HACs are summarised in Table 2.

A number of different YAC cloning strategies are employed:

Conventional YAC cloning approach. Figures 8A-D show the different vectors used for cloning DNA as YACs by the conventional restriction/ligation methods. These YACs can then be shuttled into mammalian cells and tested for HAC function.

ALU-ALU circular TAR cloning approach. Transformation-associated recombination (TAR) in the yeast *S. cerevisiae*, is a method for constructing linear and circular YACs from mammalian DNA (Larionov *et al.*, 1996a, 1996b). The recombination process is shown in Figure 9. Briefly, the technique involves the use of a vector (pVC39-AAH2, Fig. 8E) lacking an autonomous replicating sequence (ARS) but containing a functional yeast centromere (e.g. CEN6) and selectable marker (e.g. HIS3), and two ALU DNA hooks to trap mammalian DNA by recombination at ALU sequences after co-transformation of linearized vector and high molecular weight DNA into yeast spheroplasts and followed by selection on medium lacking histidine. The key to the process is that the mammalian DNA provides an ARS (11-bp sequence found frequently in mammalian DNA) which allows the HIS$^+$/CEN vector to replicate as a circular YAC. These YACs are very stable and range in size from 100 kb to greater than 600 kb (Larionov *et al.*, 1996b).

pVC39-AAH2 vector is used to clone DNA from hybrid BE2CI-18-5f to make YACs with an average insert of 250 kb. This TAR vector is further modified to create pAAH-TCNa (Fig. 8G)

so that it has the ability to shuttle between yeast and mammalian cells (as outlined in Figure 10), including the potential to expose human telomeres (TEL) at each end of a cloned fragment using a unique restriction site I-SceI.

Semi-specific and specific circular TAR. A modified circular TAR method utilising two specific 5′C and 3′C DNA hooks (300-700 bp in size) may be used to clone a specific human DNA at a frequency of 3/1000 HIS^+ transformants. The inventors prepared the vectors pVC39-ALU/C3-F2(+/-) and pTCN-TCS (Table 2) to perform semi-specific and specific TAR cloning, respectively.

The Semi-specific TAR methodology is a modification of a specific circular TAR strategy which permits the site directed isolation of target chromosomal DNA. Furthermore, in accordance with the present invention, the methodology described herein enables the site-specific cloning of target chromosomal DNA from total genomic DNA as a circular YAC at relatively high frequencies and without the need for the construction and extensive screening of complex libraries made from genomic DNA.

In a preferred embodiment of the present invention, the methodology employs a single specific DNA hook which flanks the mardel (10) chromosome and a less specific Alu-hook to trap the other side of the target DNA.

In initial experiments, a unique repeat DNA-free, 1.4kb *Eco*RI fragment (designated C3-F2) was identified from the p′ side of the 80-kb HC-contig (Fig. 11A) (du Sart *et al.*, 1997). This fragment was subcloned into the centromere-based yeast circular TAR vector, pVC39-AAH2, by replacing the existing BLUR13 *Alu* (Larionov *et al.*, 1996b) to create the pVC39-ALU/C3-F2 constructs. As the specific orientation of the C3-F2 sequence on the chromosome was not known, the fragment was cloned in two different orientations, for which the (+) orientation (Fig. 11B) was expected to trap the genomic region to the left of C3-F2, while the (-) orientation was expected to trap the region to the right. Both constructs were used in yeast transformation.

As a source of genomic DNA containing the neo-centromere, a somatic hybrid cell line, BE2C1-

18-5f (du Sart *et al.*, 1997), containing the mardel 10 chromosome but not the normal human chromosome 10 was used. 5µg of high-molecular-weight DNA from this cell line and 1µg of pVC39-ALU/C3-F2(+) or pVC39-Alu/C3-F2(-) (linearized with *Sma*I to expose the 0.21-kb *Alu* and 1.4-kb C3-F2 hooks) were co-transformed into 10^9 (previously prepared and stored frozen) spheroplasts of S. *cerevisiae* YPH857 which carries a HIS3 gene deletion, (Sikorski and Hieter, 1989) and grown on SD, without HIS medium, (Larionov *et al.*, 1996a;b) to yield between 10 and 100 HIS^+ colonies. Control experiments in which YPH857 was transformed with vector alone did not produce any colonies, indicating that the C3-F2 fragment lacked ARS-like sequences. Twenty TAR experiments were performed and HIS^+ colonies were picked into 96-well trays containing YPD medium (supplemented with 50µg/ml ampicillin and 15µg/ml tetracycline), grown at 30°C with aeration for 24h and stored in 20% (v/v) glycerol at -70°C. Total yeast DNA was prepared in pools of 48 (Kwiatkowski jr *et al.*, 1990) and screened by PCR with the primers norm 5 and norm 7 (Table 3) which are located 30-kb q' of C3-F2 (Fig. 11A). Two desired positive clones, designated 5f-52-E8 and 5f-38-F2, which contained the neo-centromere DNA derived from mardel 10 and mardel (10) and the DNA immediately p' of the neocentromeric DNA, respectively, were identified. For subsequent studies, these clones were grown on SD without HIS medium and single colonies were re-isolated for characterization.

Initially, the sequence nature and sizes of the 5f-52-E8 and 5f-38-F2 insert DNA were determined. High-molecular-weight DNA was prepared in agarose blocks and digested with an enzyme (*Srf*I) that linearized with YAC (Fig. 11A). The linearized DNA, as well as uncut intact DNA, were resolved by pulsed-field gel electrophoresis (PFGE), transferred onto a nylon membrane and probed with radiolabelled PAC4, a P1-derived artificial chromosome clone containing a 120-kb insert that spans the entire HC-contig from normal chromosome 10, (du Sart *et al.*, 1997) following preannealing with human placental DNA to suppress repetitive DNA. The intact 5f-52-E8 and 5f-38-F2 remained trapped in the electrophoretic wells and the linearized DNA migrated into the gel and demonstrated a size of approximately 110 kbp and 80 kbp, suggesting insert sizes of about 105 kbp and 75 kbp, respectively (given that the vector size is 5.9 kb).

Despite the use of a genomic DNA source previously shown by sequence-tag-site (STS) analysis

to be free from normal chromosome 10 material, it is desirable to independently confirm the mardel (10) -origin of the 5f-52-E8 YAC clone. This was achieved using a set of primers (norm 17 and 18; Fig. 11A) that detected a variable-number-tandem repeat (VNTR) region within the HC-contig/neocentromere region. The results clearly indicated the presence of a 1.4-kb PCR product that was specific for the mardel (10) chromosome (Table 3).

PCR was used to further compare the 5f-52-E8 DNA with the previously cloned HC-contig sequence derived from normal chromosome 10. PCR products with sizes ranging between 0.2 and 15.9 kb were generated by standard PCR or with the Expand Long Template PCR system (Boehringer-Manneheim). Products greater than 1 kb were digested with frequent cutting enzymes, *Rsa*I and *Bsi*XI, and their fingerprints were compared by agarose gel electrophoresis. The results, shown in Table 3, indicated the absence of any detectable difference between the 5f-52-E8 DNA and those of the corresponding regions of the normal chromosome 10 (in somatic cell hybrid BE2C1-18-1f) and the neocentromere region of mardel (10) (in somatic cell hybrid BE2C1-18-5f). These results also demonstrated that the YAC 5f-52-E8 spanned at least 75 kb of the HC-contig region (Fig. 11C), consistent with the size determined by PFGE. Furthermore, the ability of all the internal primers to amplify DNA from 5f-52-E8 strongly suggested that the YAC was not chimeric. This result was confirmed by isolating DNA from four single-colony isolates of 5f-52-E8, digesting these with *Eco*RI and *Eco*RV, and probing with radiolabelled PAC4. The hybridization patterns obtained with these enzymes were consistent with those established in the previous study (du Sart *et al.*, 1997). Thus, this analysis, based on cloned DNA derived directly from mardel 10, has provided confirmation that the neocentromere DNA region is structurally identical to that of the corresponding HC-contig region of the normal chromosome 10 (du Sart *et al.*, 1997).

The circular YACs 5f-52-E8 and 5f-38-F2 were further retrofitted with the yeast-bacterial-mammalian cells shuttle vector BRV1 as previously described (Larionov *et al.*, 1997). The resulting BAC clones were designated BAC/E8-1 and BAC/F2-14, respectively (Fig. 11D).

The specific TAR strategy is outlined in Figure 12 and uses unique fragments from the HC-contig region, such as the ends of PAC4 (a 120 kb-insert PAC clone containing the HC-region)

to create the YAC/HAC shuttle vector pTCN-TCS. An example of a YAC/HAC construct containing the HC-contig region of normal chromosome 10 is shown in Fig 13.

Completed constructs are transfected into different cultured mammalian or chicken cells (see above) by lipofection using Transfectam or DOSPER.

***In vivo* "cloning" of HC-region into HAC vectors**

This strategy employs a technique known as Telomere Associated Chromosomal Truncation (TACT) (Fig. 14). The technique is based on the principle that cloned mammalian telomeric DNA when reintroduced into a mammalian cell can seed the formation of a new telomere at an intrachromosomal location. If the introduced telomeric DNA is targeted to a known site through homologous recombination, integration at that location and subsequent truncation of distal sequences on the original chromomosomal arm can result (Brown *et al.*, 1994; Farr *et al.*, 1995). This technique is employed in our own study to truncate the mardel 10 chromosome on either side of the HC-contig/core centromeric DNA element to produce *in vivo* a stable HAC of minimal size.

Figure 15A shows an example of TACT-construct used in our study. Key features of this construct are: (a) Cloning of the pericentric human genomic DNA in both orientations (+/-). This is necessary since we do not know the chromosomal orientation of this DNA. This DNA is used to target the human telomeric sequences to locations on either side of the HC-contig region on mardel 10. Genomic DNA is derived from several different sources including Y2C24, Y3C64, Y3C109, Y3C94, Y13C12, Y13C15, Y17C6, Y17C8. The resulting truncation derivatives produced using these genomic DNAs will vary in size accordingly. (b) The termini contain 2.4 kilobases of tandem repeat human telomeric DNA (htel). This DNA has been shown previously to act as a substrate for mammalian telomerase to allow seeding of a complete telomere tens of kilobases in length. (c) The hygromycin (Hyg) resistance gene allows for positive selection of mammalian cell lines containing construct sequences integrated into the genome. This is the initial screening procedure. In addition, some constructs contain the neomycin phosophotransferase gene (Neo) rather than Hyg. (c) The Herpes simplex thymidine kinase (TK)

gene is used for negative selection against non homologous integration events into the genome. Those cell lines containing the TK gene can be selected against by adding the nucleoside analogue gancyclovir.

Figure 15B shows another example of TACT-construct used in our study. In addition to the features of the linearised construct shown in Fig. 15A, specific additional features are: (a) The incorporation of tandem telomeric blocks (htel.htel) since others have shown these to have the highest seeding efficiency of new telomeres in mammalian cells. (b) The incorporation of yeast selectable marker (eg. URA3), DNA origin of replication (eg. ARS), and centromere (eg. CEN6), to allow transfer and maintenance of the resulting truncation derivatives into yeast. This should facilitate further characterisation and manipulation, such as the introduction of therapeutic genes for gene therapy purposes. (c) The relocation of the TK gene adjacent to the genomic DNA to increase the effectiveness of the negative selection system. (d) The human growth hormone (GH) gene has been included to allow proof of principle that human genes can be introduced into a HAC and expressed under the control of endogenous regulatory elements. This is essential for gene therapy applications of the resulting HAC. (e) A CMV promoter upstream of a P1 phage loxP site (CMV/loxP) has been included to allow introduction of large human genes into a HAC *in vivo*. A plasmid containing a gene of interest, a second loxP site and a promoterless selectable marker gene is introduced into a mammalian cell line containing the HAC. Transient expression of CRE recombinase results in recombination between the two loxP sites within the cell, thereby integrating the introduced plasmid into the HAC and placing the selectable marker gene next to the CMV promoter to allow for marker selection.

For chromosomal truncation, the above TACT-constructs are transfected into a somatic cell hybrid line BE2CI-18-5f containing the mardel (10) chromosome. Positive selection is applied for Hygromycin or Geneticin resistance whereas negative selection is applied against the Thymidine Kinase Gene. Resulting colonies are further screened with distal p′ and q′ DNA fragments to ascertain the presence or absence of the two mardel 10 chromosome arms. In addition to the BE2CI-18-5f cell line, a human/chicken somatic cell hybrid line (derived from the recombination-proficient DT40 chicken cell line; Dieken *et al.*, 1996) containing the mardel (10) chromosome will also be generated and used.

EXAMPLE 16

Analysis of HAC

Irrespective of which of the approaches described above is used, the presence of a new product in a mammalian cell line as an extrachromosomal, artificial chromosome, will be assessed by fluorescence in situ hybridisation (FISH) analysis, as well as tested by extracting high molecular weight DNA to determine independently existing chromosomal entity on pulsed field gel. The stability of the construct through successive cell division, both in the presence and absence of drug-resistance selection, will be determined. The presence of the construct, in all or a high percentage of the original transfected cells indicates stability. Demonstration of this stability indicates the successful creation of a HAC.

EXAMPLE 17

Production of HAC

This example describes the use of the neocentromere as a source of centromeric DNA in the "bottom-up" approach to produce HACs in human cell culture. Bacterial artificial chromosomes (BACs) containing cloned neocentromeric DNA and a selectable marker were co-transfected with human telomeric DNA into human HT1080 cells to yield independent HACs that were single-copy and stable in the absence of selection. The properties of these HACs, and their potential utility as a new, improved vector system for gene therapy are described.

EXPERIMENTAL PROTOCOL

Preparation of DNA. Highly-purified BAC DNA was prepared using Qiagen columns according to the manufacturer's instructions. Prior to transfection, BACs were linearized with *Sgr*AI in the presence of 2.5 mM spermidine and examined by pulsed-field gel electrophoresis. Human telomeric DNA was gel-purified as a 1.6-kb *Bam*HI/*Bgl*II fragment from pSXneo270T2AG3 (Bianchi *et al.*, 1997). High-molecular-weight genomic DNA was prepared from cultured cell lines using standard methods (du Sart *et al.*, 1997).

Transfection of HT1080 cells. Transfection of human fibrosarcoma cell line HT1080 (Rasheed *et al.*, 1974) was performed using the DOPSER liposomal transfection reagent (Boehringer-Mannheim). The day before transfection, 6-well trays (each well is 962 mm^2) were seeded with 3×10^5 HT1080 cells per well and grown at 37°C, 5% CO_2. Different combinations containing 1-2 µg of each BAC, 50 ng of telomeric DNA, 100 ng of each PAC-1, 4 and 5 (du Sart *et al.*, 1997) and 50 ng of human genomic DNA were prepared in 50 µl of HBS (20 mM HEPES, 150 mM NaCl) supplemented with 0.075 mM spermidine and 0.030 mM spermine. These DNA cocktails were mixed with 50 µl of 0.4 µg/µl DOPSER (diluted in HBS) and left at room temperature for 15 to 20 min. The HT1080 cells were washed with PBS (phosphate buffered saline) and 1 ml of serum-free DMEM (Dulbecco's modified Eagles medium) was placed in each well. The DNA-DOPSER mixture was then added dropwise with swirling and the cells were incubated for 6 h. 1 ml of DMEM and 20% v/v fetal calf serum (FCS) was then added and the cells left for 24 h at 37°C, 5% v/v CO_2.The cells were harvested and seeded into 48-well cluster trays (each well is 100 mm^2) containing DMEM-10% v/v FCS supplemented with Geneticin (G418, Gibco-BRL) at 250 µg/ml. The media was changed every 3 to 4 days. G418-resistant colonies normally appeared 10 to 14 days after transfection. These colonies were expanded into duplicate 6-well trays, where the cells of one tray were stored frozen in liquid N_2, and the remaining cells were analysed by fluorescence *in situ* hybridization (FISH).

Cell culture and mitotic stability. HT1080 cells were grown in DMEM supplemented with 10% v/v FCS, penicillin/streptomycin, and glutamine. The mitotic stability of HAC containing clones was determined by growth in 25 cm^2 flasks in the presence (200-250 µg/ml) or absence of G418 selection, and grown to confluency (3-4 days) and split 1/5 and 1/10, respectively. Aliquots of each culture were harvested fortnightly and analysed by FISH (20-50 metaphases) with BAC/E8 and/or BAC/F2 probes.

FISH, ANTI-CEN/FISH and PRINS/FISH. Fluorescence *in situ* hybridization (FISH) analysis of HT1080 clones was performed with BAC/E8, BAC/F2, and/or α-satellite DNA probes. Hybridization using the BAC probes were performed under high stringency whereas the α-satellite DNA probes were used in low stringency conditions (du Sart *et al.*, 1997). ANTI-

CEN/FISH analyses involved an initial immunofluorescence staining step using a CREST antibody or specific antibodies against CENP-B, CENP-C, or CENP-E, followed by FISH using the probes described above, essentially as previously described (du Sart *et al.*, 1997).

Results

HAC construction strategy. The basic strategy involved the co-transfection of the 10q25.2 neocentromere DNA with human telomeric DNA into human cells. The neocentromere region is cloned as two, circular YACs in *Saccharomyces cerevisiae*. To facilitate handling and purification of the cloned DNA in large quantities, these YACs are retrofitted into BACs and maintained episomally in *E. coli* as circular molecules. One of the BAC clones, BAC/E8, is 120 kb in size and has an insert of 105 kb that encompassed 70 kb of the 80-kb core NC-DNA region (Fig. 16). The second BAC clone, BAC/F2, has an insert size of 75 kb that overlapped BAC/E8 by 1.4 kb, and contains ~10 kb of the core NC-DNA while extending ~65 kb into the p'-side of the mardel (10) chromosome (Fig. 16). The BAC vector backbone further contains the neomycin-resistance (Neo^R) gene to allow selection in mammalian cells. BAC/E8 and BAC/F2, used either on their own, in combination with each other or with additional DNA are used in the following transfection experiments.

Transfection of HT1080 cells. The human cell line HT1080 (Rasheed *et al.*, 1974) is chosen for the transfection experiments because of its near-diploid karyotype, its high level of telomerase activity (Holt *et al.*, 1997), and its demonstrated ability to form microchromosomes containing *de novo* centromeres from transfected arrays of α-satellite DNA and human telomeric DNA (Harrington *et al.*, 1997; Ikeno *et al.*, 1998). The resulting G418-resistant clones are analyzed by FISH and classified into different categories of events.

Transfected cell lines are designated HT-38, HT-47, HT-54, HT-190, and HT-191.

Those skilled in the art will appreciate that the invention described herein is susceptible to variation and modifications other than those specifically described. It is to be understood that the invention includes all such variations and modifications. The invention also includes all of the

steps, features, compositions and compounds referred to or indicated in this specification, individually or collectively, and any and all combinations of any two or more said steps or features.

TABLE 1

Restriction analysis of the genomic DNA of patient BE and those of his parents using three overlapping cosmids that span the marker centromere.

	Y7C14	Y6C10	Y4C7
NotI	n.a.	910	910
BssHII	n.a.	815, 340	n.a.
BsiWI	n.a.	740	740
SalI	410	410	410, 540
ClaI	315, 145, 110, 80	315, 145, 110, 80	315, 145, 110, 80
SnaBI	n.a.	250, 148	n.a.
NaeI	240, 210, 155, 120	240, 210, 155, 120	240, 210, 155, 120
NarI	222, 108, 70	222, 108	222, 200, 108, 70
EclXI	180	180	180
SfiI	170	170	170
KspI	168	168	168
AatII	165, 146	165, 146	165, 146
NheI	38	38	38
BstBI	n.a.	35	35
SmaI	n.a.	90, 40, 22	90, 40, 22
BglI	25	25, 7.2, 6.2	25
PacI	n.a.	25	n.a.
BamHI	24, 19, 15	24, 22*	24, 22*
KpnI	23	23	23, 19
BclI	21	21	21
PstI	9.4, 5.9, 5.1, 4.2, 3.8, 3.3, 2.9, 2.4	9.4, 3.8, 2.9, 2.7, 2.4, 1.5, 1.1	9.4, 7.1, 4.2, 3.3, 2.9, 2.7, 1.9, 1.5, 1.1
XbaI	14	14, 10	10
EaeI	n.a.	15, 12, 8, 6	n.a.
SphI	16, 7.5	16	16, 9
PvuII	14, 7.5	7.5, 6	7.5, 6
HindII	8.6, 6.9, 6.2, 2.7, 1.8, 1.2	6.9, 6.2, 5.6, 5.2, 5, 2.7, 1.9, 1.8, 1.7, 1.2, 0.6	6.2, 5.6, 5.2, 4.3, 2.9, 1.7, 1.2
ApaI	15, 8.5	15	15
EcoRI	11, 4.3, 3.9, 1.9, 1.5	11, 4, 3, 2, 1.9, 1.7, 1.5	10.2, 7.6, 3, 2, 1.9, 1.7, 1.5
HpaII	5.5, 4.3, 3.6, 1.6	6.9, 3.6, 2.8, 1.6, 1.2	3.6, 2.8, 2.5, 1.6, 1.2

MspI	3.9, 3.0, 2.8, 2.5, 2, 1.6, 1.2	3.9, 3.6, 2.8, 2.5, 2.2, 1.6, 1.5, 1.3, 1.2, 0.9	3.6, 3.2, 2.8, 2.5, 2.2, 1.6, 1.5, 1.2, 1
SspI	n.a.	10	n.a.
XhoII	7.5	n.a.	n.a.
DraI	7.5	7.5	7.5
BglII	8.5, 6, 5, 4.7, 3.5, 2.5	6, 5, 4.7, 2.5, 1.6, 1.5, 1	7, 6, 5, 4.7, 2.5, 1.6, 1.5, 1.1, 1
AvaII	7.4, 3.7, 3.4, 2.8, 2.6, 1.8, 1.7, 1.4, 1.2, 1.1	3.7, 2.8, 2.6, 1.8, 1.7, 1.4, 1.2, 1.1, 0.9, 0.8, 0.5	4.3, 3.7, 2.8, 2.6, 1.8, 1.7, 1.4, 1.2
StuI	12.5, 8, 7.5	12.5, 9, 8.5	9, 8.5
HindIII	6.6, 5.4, 4.7, 4.4, 2.9, 2.5	5, 4.7, 4.4, 4.1, 2.9, 2.5, 0.7	5, 4.7, 4.1, 3.1, 2.5, 2.3, 1.9

n.a.= data not available.The values represent restriction fragment lengths in kilobases. Multiple values for an enzyme denote different bands detected by a cosmid probe on a gel lane. Since there were no detectable differences between the DNA of patient BE and those of his parents in any of the fragments (except for a BamHI polymorphic band found in one of the parents, indicated by an asterisk), only one set of values is shown for all three genomic DNA.

TABLE 2

Table 2. Vectors for cloning centromeric regions from normal chromosome 10 or mardel (10) DNA into yeast artificial chromosomes (YACs). These YACs can be shuttled into mammalian cells to test for function as HACs.

Vector:	Key Feature(s)	Map
pJS97ARTi	hTEL/I-SceI/yTEL, DHFR	Fig.8A
pJS98ANTi	hTEL/I-SceI/yTEL, neo	Fig.8B
Fragmentation 1	hTEL/I-SceI/yTEL, hyg	Fig.8C
Fragmentation 2 (-/+ hGH)	hTEL/I-SceI/yTEL, neo, hGH	Fig.8D
pVC39-AAH2	ALU-ALU TAR vector	Fig.8E
pTEL/CAT/TEL	hTEL/I-SceI/hTEL/neo	Fig.8F
pAAH/TCNa	TAR vector with hTEL/I-SceI/hTEL/neo	Fig.8G
pVC39-ALU/C3-F2(+/-)	ALU-specifc TAR vectors	Fig.8H
pTCS	ends of PAC4 in pBS	Fig.8I
pTCN-TCS	specific TAR vector hTEL/I-SceI/hTEL/neo	Fig.8J

TABLE 3

PCR analysis of YAC 5f-52-E8 clone and comparison with the HC-contig/neo-centromere region from normal chromosome 10 and mar del (10)

Primer-Pairs [a]	Genomic DNA used in PCR (product size in kb)		
	BE2C1-18-1f[b]	BE2C1-18-5f[b]	YAC 5f-52-E8
norm: 141 + 55	1.80	1.80	not present
norm: 32 + 30	0.90	0.90	0.90
norm: 28 + 29	1.00	1.00	1.00
norm: 1 + 3	2.90	2.90	2.90
norm: 39 + 52	1.20	1.20	1.20
norm: 5 + 7	0.23	0.23	0.23
norm: 16 + 5	3.50	3.50	3.50
norm: 9+ 14	0.90	0.90	0.90
norm: 36 + 37	2.00	2.00	2.00
norm: 168 + 71	4.00	4.00	4.00
norm: 27 + 10	15.90	15.90	15.90
norm: 18 + 17 (VNTR)[c]	1.20	1.40	1.40
norm: 68 + 17	8.00	8.00	8.00
norm: 34 + 47	3.00	3.00	3.00
PAC4t7: a + b	0.30	0.30	not present
AFM259xg5: ca + gt[c]	0.21	0.19	not present

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[a] Refer to Fig. 1a for the relative positions of each primer-pair.

[b] BE2C1-18-1f and BE2C1-18-5f are somatic hybrid cell lines containing the normal human chromosome 10 and mar del (10), respectively (2).

[c] The 'norm: 18 + 17' and 'AFM259xg5: ca and gt' primer sets allow distinction between the normal human chromosome 10 and mar del (10) by detecting a VNTR and a microsatellite, respectively.

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SEQUENCE LISTING

(1) GENERAL INFORMATION:

(i) APPLICANT: (US ONLY) CHOO, Kong-Hong Andy, DU SART, Desirēe and CANCILLA, Michael Robert
(OTHER THAN US) AMRAD OPERATIONS PTY LTD

(ii) TITLE OF INVENTION: A NOVEL NUCLEIC ACID MOLECULE

(iii) NUMBER OF SEQUENCES: 29

(iv) CORRESPONDENCE ADDRESS:
(A) ADDRESSEE: DAVIES COLLISON CAVE
(B) STREET: 1 LITTLE COLLINS STREET
(C) CITY: MELBOURNE
(D) STATE: VICTORIA
(E) COUNTRY: AUSTRALIA
(F) ZIP: 3000

(v) COMPUTER READABLE FORM:
(A) MEDIUM TYPE: Floppy disk
(B) COMPUTER: IBM PC compatible
(C) OPERATING SYSTEM: PC-DOS/MS-DOS
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(viii) ATTORNEY/AGENT INFORMATION:
(A) NAME: HUGHES DR, E JOHN L
(C) REFERENCE/DOCKET NUMBER: EJH/AF

(ix) TELECOMMUNICATION INFORMATION:
(A) TELEPHONE: +61 3 9254 2777
(B) TELEFAX: +61 3 9254 2770

(2) INFORMATION FOR SEQ ID NO:1:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 19 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

GGATTACAGG (C/T)(A/G)TGAGCCA 19

(2) INFORMATION FOR SEQ ID NO:2:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 19 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

(A/G)CCA(C/T)TGCAC TGCAGCCTG 19

(2) INFORMATION FOR SEQ ID NO:3a:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 40917 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3a:

GAATTCTCCT GCCTCAGCCT CCCAAGTAGC TGAGGTTACA GGTGCCAGCC ACCACGTCCA 60

GCTAATTTTT GTATTTTAGT AGAGACGGGG TTTCACCGTG TTTGCCAGGC TGGTATCAAA 120

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CTTTGACCAT TTTCTTTAGT ACTGAATACT TTTTTTGTAT TTCATTATAT CTATTGGCTT 720

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(2) INFORMATION FOR SEQ ID NO:3b:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 39678 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3b:

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GTCATTCTGC CAGAATTC 39678

(2) INFORMATION FOR SEQ ID NO:4a:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 41008 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4a:

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GGGGAGTGCA CGCCTGTGTT AAAGGACA 41008

(2) INFORMATION FOR SEQ ID NO:4b:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 39238 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4b:

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(2) INFORMATION FOR SEQ ID NO:5:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 5596 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

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CCGCGTGGAC TCACAG 5596

(2) INFORMATION FOR SEQ ID NO:6:

(i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 18443 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

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CCTCTCTTTC TTTTAGGGAA ATGCTACCCA CTCTTTGCAT GGGTTCTGGA TGGAACTGTT 240

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GCCGCCACCG CGGTGGACTA GAT 18443

(2) INFORMATION FOR SEQ ID NO:7:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 11811 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

CCTGTTAAAG TTTACCTTGT ATCTTAAAAC TTGCCCTAAC CGGATTAATT TTCTGGCCAA 60

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CTGCTAATAC TGTCTTAAAT ATGGTAGCTA TATAGTAAGC CTTAACACTG AGTAGATAGA 7260

TTTCTCCCCT TTTTTTGTTC TTTTTCAAAA TTGTCACTGG TTTGTTTTTA TTTTTTACTT 7320

TATGCAGATA ATCTGTACTA TACTTTGGTT TCATGTATCA AGTAGTTTGT TCCAAGTTGT 7380

GCTTTAAGCA GAACAAATAA ATTTTCATAT TGTTCTTTGT GTTAATCTGC AATATAAACC 7440

TATACCAAAT TCTATTTTGT GTATTTGTTT ATTGTAGTAA TCTGACTGAC TCTTTTGCCT 7500

CCAGACTCAT CTCTTTCAAG GTCCCCAACT GAATCTTGTT TTAGGTGGAA CTTAGAAGCA 7560

GTAGAAGTTA AGAATCTATT TCACAGCCTT AGTAGTCTAG TTTCATTCTC TATATAATGT 7620

TGTCTATGCA AGTGAGCTGC TCTCCAGTGC CTTAGTTTCA CTAATGTTGG GGAAGGTCTC 7680

TTCTCTTGTT TTGGACTTCT CTATCACATT GCCTTTCTCA AGAGAAGACA TATAATGAAA 7740

GTTGATATCT GGTGTTCTAG GACTTCTTCA GAAGCTTGCC AGTTTTTCAA GCTGATTTCT 7800

CTCACTGGCA ACTCTTCAGA GTGCTGTTCC TACTCCACCC TCCCCTGGTG GTATGTATCA 7860

GTTTTCTACT CATCAGCACC CACCTACTCC TGCCTACTGT GTTTCTCAGA TGTCTGCTGC 7920

CTGGCTAGCT CATTGCTGCT TTTGTCACTC ATAGAGCTGT CTTCTTCCCT TTTTTTGGCT 7980

TTCTGCCTGA CTTCCAGGGC AGCTGCTCTG TCATTGCCTG TCTGCCATTC TGTCTTTTTT 8040

CCCCCTACCC CCCACAGATA CAACATCTAC TCTAATACCA CACATTCTCC ATGTTCAAAC 8100

TAACCTCATC ACTTTCCCCA CCACATTCCC CAAAACTGGT CATCCTCCAG CTTATAGCAT 8160

TGCAGTTCAC TGAAGTTAGA CATCTGGGCC TTGCTTACCT CCAACATCTC ATTAGCCTTC 8220

GATTCTACCC CTATAAATCC TCTTCTCAGT CTCCTTTAGA TATTCCTGCC CTGCTGTGAG 8280

ATCCATCTGG TTTATTGGCT AGATTACTTC AGAAAGCTTC AGTCAGTGAC CCTCCTTACT 8340

TCAAACCCCA CCAGTTGATC CTTCACTCTG CCATCAGTCA TTGCTTCTAA AATCTAAATT 8400

GTTCCATTTA ACCTTGCTGT GATAAAACCT TTGGTAGTTC TTCAGTGTGT TCAGTGGTAA 8460

GTTAAAACTT TCACTGTAAT GTACAGGCCC CTTCATGATA TGATCGCTGC CTCCTCGAGC 8520

CTCATTGTGT GCATTTCCCC GCCCCACCCT TTCCTCACCC ACCCTAGTCT TTCATGTCTG 8580

CCATTTTTAC ATTCATTTAG CAGATATTTA TTGAAGCCCC CTGTGATGTC CTTACCTAGG 8640

TCTTTCTTGT TGCCAGGACC AGACAGGCTT TTTCAAGCTT CCAAGTCATC TCAGTTTGAA 8700

AGACTATGTC TGACCCTTGT CTTGGCCAAT TACTCTTTAT CCTTCCAAGT TCAATGATTG 8760

TCCCACTGCA CTCCAACCAG AGTGAGAGAG CAAGACCCTG TCTCAGTAAA TAAAAATAAA 8820

TAAATAAATA AATAAATAAA TAAATAAATC AGCCATAATT TATTTAATCA TGTCTCTCTC 8880

CCCCATTGAT AGACGTTAAG GGTATTTCCA GTATTCTTCT CTTGAAAACA ATGCTACATT 8940

GAATAACCTT GTACATGGGT CACTTTGAAA GTATGGATAT GTATCCGTGG AATAAGTTTC 9000

CAGAAGTGGA ATTGTGTCAG AGGGGTTGTG CATTTGTAAT TCTGATGAAT ATTTATAGAT 9060

TATATGAGAG TACCTGTTTA CTCAAACTCT TGCCAATGCA GCATTATCAA AGTTTTTTAT 9120

GTTCGCCAGT GTGATAGATT AAAAAATGGT ATCTCAGCCA GGCGCAGTGG CTCACGCCTG 9180

TAATCCCAGC ACTTTGGGAG GCTGAGGCGG GCAGATCACG GGGTCAGGAG ATCGAGACCA 9240

TCCTGGCCAA CACAGTGAAA CCCTGTCTCT ACTAAAAATA CAAAAAATTA TCCAGGCGTG 9300

GTGGCGGGCA CCTGTAGTCC CAGCTACTCG GAAGGCTGAG GCAGGAGAAT GGCATGAACC 9360

TGGGAGGCGG AGCTTGCACT GAGCCGAGAT CGCGCCACAA CATTCGAGCC TGGGCGACAG 9420

AGCGAGACTC CGTCTCAAAT AATAAAAAAA AAAGATGGTA TCTCAGCATT GATTTCTTTG 9480

ATCATCAGTG AGGTTGAGCA TCTTTTCATA GATTTAAGAG AACTGTATGG TTTTTTGTGA 9540

GTTATGTTTC ATATCGTTTA CCCATTTTAC TTTTAGGCTG GAAGCAGCTG TTTTAGTGGA 9600

ATGGTGGAAC AAGAAGCCAG ATTGCCATGG AGAGACAACT CTTTCTAGAG ATTTGGCTAT 9660

GAAGCAGAGT AGAGACAATG ATAGCTGAAG GATTGATGTA GATGCAAAGA AATTTTTCAT 9720

CTTCTTTGAA AACTTAATTG TGTTAAAAAC TGGTATGAAA GGGAGGGGTT AAAGCTAGAG 9780

ATGGTGGTAG AAAAAAATGC AGGGTTCCTA AAGGACTGAG ATTCCTGGAT GGAATTTCAG 9840

GGAAGGGGAA AATTTCTGGA TATAGTGACT GGGGAGTTAA GGGTGTCTAG TCCAATGGCT 9900

TTTATTTTCT TGGAAGGGTA GGCAAGGCCA ACAGCCACAT GTGTGGGAGG AGATGGTTAG 9960

AGGGGAGAGG AGGTTTGAAG GCACCGCTAT GGAGAATTGG AGAGAGCTAA GGAAAGACAG 10020

AAAGACTGCA GAAAGTGCTT AGGGTTCCAC TGAAGCGGAA ATAGTGATTT GTAGTGATAC 10080

AACCCTTATG AGTTATTTGA TTTTTTTTTT TTTTTAAGCA GCATCTGGCA GTCCAAGTAT 10140

AGGGCTGACA GTTTGGGATT TTTCTTTCCA TGTTGGTGTA AAAGAAGAAC AGTGTAGTGA 10200

AGGAAGTTAG GACAAAAGAA TGATTGAACT GACACCAAGT TTTCTTGATT TGGTAGAAAA 10260

GGAAATAAAG ATAGAGCAGA GATATTGAAA AGAATTAGAG AGGGGTTCAA GAGACTGAAG 10320

GCCTGGGTGA GGTCAGAGAG CAGGTGTGGT AGACATAACA GAGAGAACTA CAAGGATAGA 10380

AAGTGTGGTT GGAGAGTGGG AAGGCAAGAT TTATTCAGTA TGGGGGCTTT TCTGGGTGAT 10440

GACAGCATCT GGAGTACAGC CATTGTCGTG AGTGGCCCAA GTGTAGCAGA GATAAAGCGT 10500

TGTTGGAGTG AAGGAAGTCA AGGAACTGAG AGGCTGGCCT AGATGGGGAT TTTGGTTGTC 10560

ATCCATGAGG ATATTGAAGT CATCCAGGAG AATAGCAGGC CTGGGGGACA GGAAGGAAAC 10620

TGAGCCACTT ACAGTGTCTT CAGTGATAGG AAAGCACAGG GCAAAAAGCT TTCAAGAACA 10680

GGGACTGTTA AGCCGGGTAC AGTGGCTCAC ACCTATAATC CTAGCATTTT GGGAGGCCAA 10740

GGCGGGTGGA TCACTTGAGG TCAGGAGTTC AAGACCAGCC TGGCCAACAT GGTGAAACCC 10800

CATCTCTACT AAAAATACAA AAATTAGCCA GGCATGGTGG CACGCGCCTG TAATCCCAGC 10860

TACTTGGGAG GCTGAGGCAG GAGAATTGCT TGAACCTAGG AGGCGGAGGT GGCAGTGAGC 10920

CTAGATCGCG CCCTTGGCTG CGATCCAGAC TTCACTCCAG CCTGGGTGAC AGAGCAAGAC 10980

TCTGTCTCAA AAAAAAAAAA GAAAATCAGA CTCTTAATAT TTGTAAAGAA GTAGTCCTTG 11040

AGCTACTACT TAAGTCTAGA AAGAGTTGAT ATTCTTGTTT TAAGAGTGTT AGGGCACTTT 11100

GGGAGGCTGA GGCAGGTGGA TCACTTGAGC CCAGGAGTTC CAGACCAGCC TGAGCAATAT 11160

GGGGAAACCT TGTCTCTACT AAAAATACAA AAATTAACCA GGCATGTGGT ACGTACCTGT 11220

AGTCCCAGCC ACTTGGGACG CTGAGGTGGG AGGATCACCT GAGCCCAGGA AATGGAGGTT 11280

GCAGTGAGCC AAGATTGCGT GACTGTACTC TAGCCTGGGC AACAGAGCAA GACTCTGTCT 11340

CAAAAAAAAA AAGGGCGGGG ATTATCATAG TGCCATTATT ATTATGAGTT TATGATGGCT 11400

TTCTCTAAGC ACCTTTTACA TTCGGCATTT ATTCAGTACC TATTAAGCAT CAAGGAGTCC 11460

AGAAAAAATT TTATATATAA ATATATATAA AATATGTAAA TATATATATG CATATGCTTC 11520

CCTATCTCAG GAAGGAAATA TGTGAACATC AGGAACCGAA GTCTACTCAG TTACATGCCA 11580

TTGGATATAT CACACAAAGT GCTGAGGGAA CTCAGAAGGC TCATTATATC TGGGGAGTGG 11640

GAAGGAGGCA CAGAGATGTG CTTTGGGAAG TTTAAATTAA AATAGCAAAT GGGGAAAATG 11700

AAGACACACC AGACAGGGCA CAAGCAAAGA GACATGAAAG AGTAAGTCAT GTGTTTGAGG 11760

ATCTGGGGAT CCACTAGTTC TAGAGCGGCC GCCACCGCGT AGCAGTTACG G 11811

(2) INFORMATION FOR SEQ ID NO:8:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1241 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

TCGTGATGCG GTATTTTCTC CTTACGCATC TGTGCGGTAT TTCACACCGC ATAGATCCGT 60

CGAGTTCAAG AGAAAAAAAA AGAAAAAGCA AAAAGAAAAA AGGAAAGCGC GCCTCGTTCA 120

GAATGACACG TATAGAATGA TGCATTACCT TGTCATCTTC AGTATCATAC TGTTCGTATA 180

CATACTTACT GACATTCATA GGTATACATA TATACACATG TATATATATC GTATGCTGCA 240

GCTTTAAATA ATCGGTGTCA CTACATAAGA ACACCTTTGG TGGAGGGAAC ATCGTTGGTA 300

CCATTGGGCG AGGTGGCTTC TCTTATGGCA ACCGCAAGAG CCTTGAACGC ACTCTCACTA 360

CGGTGATGAT CATTCTTGCC TCGCAGACAA TCAACGTGGA GGGTAATTCT GCTAGCCTCT 420

GCAAAGCTTT CAAGAAAATG CGGGATCATC TCGCAAGAGA GATCTCCTAC TTTCTCCCTT 480

TGCAAACCAA GTTCGACAAC TGCGTACGGC CTGTTCGAAA GATCTACCAC CGCTCTGGAA 540

AGTGCCTCAT CCAAAGGCGC AAATCCTGAT CCAAACCTTT TTACTCCACG CACGGCCCCT 600

AGGGCCTCTT TAAAAGCTTG ACCGAGAGCA ATCCCGCAGT CTTCAGTGGT GTGATGGTCG 660

TCTATGTGTA AGTCACCAAT GCACTCAACG ATTAGCGACC AGCCGGAATG CTTGGCCAGA 720

GCATGTATCA TATGGTCCAG AAACCCTATA CCTGTGTGGA CGTTAATCAC TTGCGATTGT 780

GTGGCCTGTT CTGCTACTGC TTCTGCCTCT TTTTCTGGGA AGATCGAGTG CTCTATCGCT 840

AGGGGACCAC CCTTTAAAGA GATCGCAATC TGAATCTTGG TTTCATTTGT AATACGCTTT 900

ACTAGGGCTT TCTGCTCTGT CATCTTTGCC TTCGTTTATC TTGCCTGCTC ATTTTTTAGT 960

ATATTCTTCG AAGAAATCAC ATTACTTTAT ATAATGTATA ATTCATTATG TGATAATGCC 1020

AATCGCTAAG AAAAAAAAAG AGTCATCCGC TAGGTGGAAA AAAAAAAATG AAAATCATTA 1080

CCGAGGCATA AAAAAATATA GAGTGTACTA GAGGAGGCCA AGAGTAATAG AAAAAGAAAA 1140

TTGCGGGAAA GGACTGTGTT ATGACTTCCC TGACTAATGC CGTGTTCAAA CGATACCTGG 1200

CAGTGACTCC TAGCGCTCAC CAAGCTCTTA AAACGGGAAT T 1241

(2) INFORMATION FOR SEQ ID NO:9:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1701 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

ATAAAAAACA GTTAATTAGG AGTATCTAGG TTATGTGAAG CATTCATCAC CYYCCTAYTG 60

RCAGAAAWTW TCGWTAGGCA AATTTTATAT TWTAAGTAAC TTTAACATGA ACACTTCTTA 120

AACTTTGGCT CATAATTTCA CAAAAATTAG GCTGCAAGTC ACCATATTCA TCAGATACTG 180

GCAGACACTA ACTTCTGCGG CTATGACACC AAGCAATACT GAAATCTCTT ATCTTTCCAG 240

GGGGGTTGTT CATGTATTCA GTGTTTGCAA AGAGTTCCTG CTGAGCTAAA CACAGTCCAC 300

TGTGCACTCT ACGAAAGAGT CCATGAGACA AGCATGGGGG AGGGTAGGAA GTTTAATACT 360

TTCACAATGC CTGTGGAGAC GCTGGCAGTG ATGAAAGCCT AGAAAACTCA TGAAAGGACC 420

TTTTATGAGC AGGGTGAATG TAGAGCACAA AAGCAAAGTC AGATGACCCA CTTAAAGCTT 480

TGCCTTTACT GATGAGAATT CATTCTCATT CCAGATTAGT CTCTCTCTAG AAAAAGCAAA 540

CCTTATATAA GAGTTGGAAA ATTAAGATAC AGGAAGTATA ATTCTACTAA ATTCCAGTTT 600

TTCCTTCTCA AATATCAGCC TAAGTCCTAA GGTCTGTGGC CAAAGACAGA AAATACAAGG 660

CGCTGAGAAA TATGCTATTT ATCTTGGTGT AACAATCTCT GACTGTTGGG GTTTGAGGAA 720

ATTTAAGCTC TACAATCCAT AGATCAGACC AGAAGTTTAG GGTAGTAATA TTATGAGAGG 780

AAATAGTTTC TTTCTGGAAC TTATATAAAG CAAATAACTG GTAAACCTGA TTTGCAAGGT 840

AATGACAGTC CAAGTTCCTT CAAAGCAGAG AACCACTTAT TTGCTCATTC ATTCAACTAA 900

GTTCCTTGTC TTGTGCCAGG CTGGAGAGAG AAAGCAGCTC CTGTCCTCAA GGAGCTCACA 960

TCTCAGGCAT CTTCTCACCC TCCTTTCTCA TGTTAACCAA AACATTTCAG GTTCATCAAT 1020

GAAACTCTTC ATCCAGGAGG CAGATAAAAT GGCTTCTCTT CATTTTGATT CATTTACTCT 1080

TTCTTTTATT TATTTTATTA TTATTATTTT TTTTTTTTCT GAGAAGGAGT CTCGCTCTGT 1140

TGCCCAGGCT GGAGTGCAGT GGCGTGATCT CGGCTCACTG CAACCTCTGC CTCCCGGGTT 1200

CAAGCGATTC TCCTGCCTCA GCCTCCCAAG TAGCTGGGAT TACAGGCATG CGCCACCACG 1260

CCCGGCTAAT TTTTGTAATT TTAGTAGAGA TGGGGTTTCA CCATGTTGGT CAGGCTGGTG 1320

TCAAACTCCT GACCTTGTGA TCCGCCTGCC TCAGCCTCCC AAAGTGCTGG GATTACAGGT 1380

GTGAGCCACC ATGCCCGGCC TACTCTTTCT TTTAAACAGA GAAATAAGAT GGAATATTTT 1440

TATCCCATCT TTTCTTCTGT AATTAAAAAA GGAATACGAA GAAACTTGAC ATAGTCTCTC 1500

TCCTCATGTG CTCTCTTACT TCCCATCCCA ATTCCATGTT TGCTCTCTTT TTCCTCTCTC 1560

CTTCTGTTTT GTTGTGAATG AAGAATTAGG TAACTAGTCC AAAACTACAG AGCTACACCT 1620

GGAGCCTAGA TTCACTGGTA GCAAATCACT AATTTTCTGA AGGTAAATGG GAGAAAATGG 1680

GGGTGGGGGG AAACTCATTA A 1701

(2) INFORMATION FOR SEQ ID NO:10:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1293 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:

GGAGATAATA AGTATACACT ATGTGTGAAG GGGGTGTCTC TATTGTTGTT GTGGCGATTA 60

GGTGAGTAAT	TTTACACCTG	GTTGTGAATA	AAGTCCGAGA	TTGGGGGACT	CACGCTTTGT	120
AGAGTCTCCC	AGGACAATGG	GTTTTGCCCC	CGTGCCCAAT	TAATAGTTAA	AGGTTGGGGG	180
CTTTTCGATT	CCCTTATTCC	AACTGGATAG	GGCTCTTGAA	ATGCCCCCAA	AAAAGGTTGA	240
CCCTTTCCCC	ACACGTCAAA	GAGGGAATTC	TCCCGCTAGA	CTACCCTTGA	ACCTGAAGTG	300
CAGTCCCTAC	AGGGTATTCT	AGCTTGTTAG	CATCCCCCAC	TGTGAATCAA	TCCCTTAAAA	360
TAAACCTATA	TAAGATGTAT	GTAATAGAGG	ACTAATCTTT	AATATAATAA	GCATATATTT	420
AATATAATTT	CGGTACTACC	CCCTTATCTG	GGGGGGGGGT	GGGGGGATAT	GTTCCAAGAC	480
TCCCAGTAGA	TGCCTGAAAC	CACAGATGGT	ACTGAACCCT	ACGTAAACTG	TATTTCATTC	540
CTATACATGC	AGGCTATGTG	TTGTAATCTG	TAGGGTAACC	ACTAAAAGAA	CAGGGTCTAT	600
AACTTGGCAA	GAGGGAAAAA	AGCTAGGATA	GTAAAAAAGT	CTATCAATCC	AAAAAGCAAG	660
AAAAAAGAGA	AAAAGGAACA	TGCTGGCATA	TTATTATAAG	TATTGTATTT	TATTATTAGT	720
TATTGTTAAT	TTTTTACTGT	GCCTAATTTA	TAAATTAAAC	TTTATCACAG	CTATGTATGT	780
ATAGGAAAAT	ATATATCTGT	GGTTTTAGGC	ATCCACTGGG	GGTCTTGGAA	TATAATGCTT	840
CCCCCAGATA	AGAAGGTACT	ACTGTAATTA	TATTATATGT	CATATTAAGT	ATACATTAAT	900
TCTACTAGGT	AGTAGCCACA	TTATATATTA	ATTATATTAA	ATATATATCA	TATAGAATTA	960
TTTTAAGGAA	TTGACTCATA	ATAGAAGAGG	CTGGCAGGCT	GGAGATTCAG	GGAGGAGTTG	1020
CATTTCAAGT	GCAAAGGCAG	ACTGCCAGAG	AATTCCCTCT	TGCTTGGGGG	AGGTCAGCCT	1080
TTTGTTCTAT	TCAAATCTTT	GAGGAAAATA	GAAAGCAAAG	AATATATTAA	CTATATTAAA	1140
CAAACTAAAT	GTTCCAATTA	AAATACAAAA	ATTATAAAGC	CTAATAATAA	AAGCCCTCAA	1200
TTATATGCTG	TTTAAAAGAG	ACATTTTTAA	GCTTAAGGAT	ATAGAAAAGT	TGAACATACA	1260
AGCATGGAAT	AAAATAAGCA	TGCAAAATAC	TAG			1293

(2) INFORMATION FOR SEQ ID NO:11:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 529 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:

GCTGAGGTGC ATCGCGGTGG CGGACGCTCT AGAACTAGTG GATCCCCAAA CAAAACCTGT 60

CCCTGCTAAT GATGGTAGAC CCAATCAGAT CCCCGGAGAA GCCGAAATAC GGAAACCATA 120

TCAGCATACG CATGGCATAC ATAGAACCCC ATACATGGAT TGCTTACTCA GCCAGATATA 180

GAAATCTATC TTCACGATAG AGATATATAT ATATAGACAC ACTGCATATA CAGATGTGAG 240

ATGGAGGCTC ACTCTGCCAC CCGTGCTGGA TCTACAGTGG CACAAGCTCA GTCCACAGTC 300

ACGTCGATCT GCCGGGCGTG ACCGACTGAG ATGCAGCGGC CTCGGGCGTA GCTGTGAGTA 360

CACGCACCAG TCATCGCGAC TGGCTGCAAG TGGTATAAGC GGAGGGGACA GGGTTACAGC 420

ATGACGGCTA GGCAGGCCGC AAACTGAGGA CCACAAGAGT GCCACGCTGC CCGAACGCAT 480

GCAGTGGCGA GATTACATGG GGCAGCCACT AGAGCCGCCG TATCAGAAA 529

(2) INFORMATION FOR SEQ ID NO:12:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18073 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:

AGCGCGTGCG CCGCTCTAGA ACTAGTGGAT CCCCCGAGGA GTGAGGAGGA CCTCAACCCT 60

ACTTCCTGAA ATGGAGCTCT GAGATGTTGG AGTAGAAATT TGGAAACCAG AGAGAGAAGT 120

AAGGGTAGTG TTGTTGCAAC ATGCATTGTA TATGGGGGGT CGGGAAGTCA CAGGAGTTTG 180

CCTCAAAGTC TTTCTCGGAG ACGGATGAGG TTTTCACTGT GATTTTCCTG GTCGTGGTCT 240

ATGGATATAG TACCTGTTAG TGACATGGAT CTTCTTAACT TCTGATGTGT CTTTTCCTCC 300

CTAGTGTACG CATACCAATT CTCTCCACAG CTTCCATCAC CATGCATTTG TTCTTTTCCC 360

TTGTTCTTGT ATTACCTTTC TGGAAAGGAA TTTTTATTGT AGGCTAATTG TTACTCCCAC 420

CAGTATTTAA CCACTGGATA TTTCATATGA TTGATCTCTT CTGATTTGGA AAATAAAAAT 480

GTAATCTCAT TATATTCATT TGATTAGTGG GGACAGTCAA CACTTCTTTG TGTATTTTCT 540

TAGCTGTTCG TTTTTCTCGT CTGTAAATTA TCTGTTTAGG TCCTTCAGAT TTTTCAAAAT 600

TGGACTGTTA TGTTTTCAGT ATTGTTATGA GTTCTTGTTT CAATTATTTA TGACAGTTCA 660

TTTTCTTTTT TAAAATAGAC TTTTTTTTTC TTAGAGAAAT AAGAAAAAAT AAAAATTAAA 720

ATAGACTTTG TGTTTTAGAG AGTTTCAGGT TCACAGCAAA ATTGATCAAA AAGTATGGAG 780

AGTTCCGGCC AGGCGCGGTG GCTCACACCT GTAATCCCAG CACTTTGGAA GGCCAAGGTG 840

GGCAGATCAC AAGGTCAGGA GTTTAAGACC AGCCTGGCCA ATATGATGAA ACCCCATGTC 900

TACTAACAAT ACACAAATTA GCTGGGTGTG GTGGTGCACA CCTGTAACTG TACCTACTCA 960

GGAGGCTGAG GCAGAAGAAT CTCTTGAACC TGGGAGGTGG AGGTTACAGT GAGCCACAGT 1020

CATGCCCCTG CACTCCAGCC TGGGCAACAG AGTGAGACTC CGTCCTAAAA AAAGAAAGAA 1080

AGAAAATATA GAGCATTCCT AAATACCACC TGTCCCCAAC ACCTGCACAG CCTCCTCATT 1140

ATCCACATCC TACACCACTG TGGTACCTTT GTTGCAATTG ATGGACCAAC ATTGACTCCT 1200

CATTATCACC CAAGCTTTGG TGTTGTACAT TCTGTAGATT TGGACAAATG TATAATGACA 1260

TGTGTCTACC ATTGTAGTAT CATACAGAAG AATTTGACTG CCCTGACAGT CCTCTGCTCC 1320

ACCTGCTTAC TCCTCTCTCC CTTTTCCTAA CTGCACAACC ACTGATTTTT TTTTTTTTTT 1380

TTTGAGAGGG GGTCTCACTC TGTCCCCCAG GCCGGAGTGC AGTGGGGCCA TTTGGGGTCA 1440

CTGAAAGCTC CACCTCCGGG GTTAATGCAA TTCTCCGGCC TCAGCCTCCC GGGTAACTGG 1500

GATTAAAGGG GCCCGCCACC AAATCGGGGT AATTTTTGGA ATTTGAAGTA AAAAGGGGGT 1560

TTCCCCATTT TAGCCAGGAT GGTCTCGATC TCCTGACCTC GTGATCCGCC CACCTCGGCC 1620

TCCCAAAGCT GGGATTACAG GCATGAGCCA CCACGCCCTA CCTTTTTTTT AAAAAACAAG 1680

GTCTTGCTCT GTCACCCAGG CCTGAGTGCA GTGATGATCA CTCCTCACTG AAGCGTCGAC 1740

CTCCCAGGCT CAAGTGATCC TCCCACCTCA GCCTCCTAAA TAGCTGAGAC TACACACACA 1800

CACCACCATG CCCAGCTAAG TTTTGTATTT TTTATAGAAA TGTGGTCTTG CTGTGTTGTC 1860

CAGGCTGGTC TTGAACTCCT GAGTTCAAGC AATTTGCCTG CCTTGGCCTC TCAAGGTGTT 1920

GGGATTACAG GCATGAGTCA CCGCACCTGG CCTTTTTTAT TTTCTTTTTT TTTTTTTAAC 1980

CAGTGATCTT TTACTGTCTC CATGGTTTTT CACATTGGCT TCTGTCACTT AGTAATATAT 2040

GTTTAAGTTT CTTCTACGTA TTTTCATGTT TTTAGCTTAT TTCTTTTTAG CAGTGAGTAA 2100

TATTTCATTG TCTGGATGTG CCATCACTTA TTTATCCATT CGCCTGCTGA AGGATATCTT 2160

GATTGCTCCC AGTCGTGGCA ATTATAAATA AAGTTGCTGT AAACATCCAT GTGCAGGTTT 2220

TTTTTAAGTG GCATAAGTTT TCATCTCATT TGGTTAAATA CCAAGGAGCA CAATTGCTGG 2280

ATCATATGGT AAGAGCTTAT TTATTTTTTT GAGAGACTAC CAAGCTGCCT TCCAAAGTGG 2340

ATGTACCATT TTGCATTCCC ACCAGCAGTG AATGAGAGTT CCTGCTGCTC CATATTCTTA 2400

CAAACATGTA GTATTGTCAA ATGTTTTGGA TTTTAAAACC AAAATCCATT TTCATAGATG 2460

TGTAGTGGTA TCCCGTTTTA ATTTGCAATT ACCTAATGAC TTGATGTTCT GTGTCTTTTC 2520

AGATGCTTAT TTGCCGTACT GTTTATCTTC TTTGGTGAGG TGTCTATTCA GGTCTTTTGC 2580

CCATTTTTAA TCTGGTTGTT ATTTTTCTTG TTGAGTTTAA GAATTCTCTG TCCTTTGTCA 2640

GATCTATCTT TTGCAAATAT TTTCTCCTAG TCTGTGGCTT ATCCTCTGAT TCTCTTGGCA 2700

TTGTCTTTCA CAGAGTAGAC ATTTTATATT TTAATGAAGT CCAGACTATC AATTATGTTC 2760

TCATGGATCA TGCCTTTGAT GTTATATCTA AAAAGTTCTC GCCATACCCA AAGTCATCTA 2820

GATTTTCTCC TGTTATCTTC TTGGCATTTT ATAGTCTTAT GATTGATATT TAGGTCTATG 2880

ATTCATTTTT AGTTAAATTT TTGTGAAAGA TAATAAGGTC TGATATGGAT TAATTTTTCT 2940

ATATGTAGCT GTCCCGTTCC AGTATCATTT GTTGAAAAGA CTATCTTGCT CCATTTTATT 3000

GCCTTTGCTC CTTTGTCAGT TGACTATATT TATGTGGGTC TGTTTATGAT CTCTGTTCCG 3060

TTCCATTGAT CTGTTTGCCT TTTCTTTTGC TAATACCACA GTCTTAATTA CCATAGCTTT 3120

AAAGTAAGTC TTGAAGTCCA ATAGCATTAA TCTTTGACTC TTCTTTAATA TTGAGTTGCC 3180

CCTTCAGAAT CTTAATGTCT CTCCATGTAA ACTTTAGAAT CAGCATTTTT ATATTCACAA 3240

AATAACTTGC TGAGATTATG ATTGAGATTG CATTGAATCT ATAGGCTTAT TTGGGAATAA 3300

CTGACATCTT GACAATATTG AGTCTTCCTG TCCATAAACA TTATTTATGA TGGGCTTCTT 3360

CTTTATGTTT AGGAGCTTTT GTTTTTTCTG TCAGATATTC CACTTCTACC TTTATGATTT 3420

CTTAATTGCC TTTTATGCTT AGAAAGTTTT TCCTCATCCT GAGCTCACAT ATTCATTTAT 3480

TTTCTTTTAA AATGTGTTTT CAAGCATTTA ATTTTTAAAC CTATGTGGAA TTTATTTTGG 3540

TATATGGAAT GAGGTGGTGG TCTAACTCCC TCCTCTCAAA TATGTAGTTA TTTTTCCCAA 3600

AACCATTTTC TATTAATTTA TCAAGAATAG ACATGTATAC ATATACATAT ATAATAGTCA 3660

GCCTTCCACT TGTTGTTTGA CCCTTGTGAA GGAAATTGTA TGAGTTTCCA ATTTTGGATT 3720

AGGCTCAGGT AGTAATTGAG CTGGGTTCTG CCAGAGATCC ATGTTAATTC ACTATCCAAA 3780

CAGAGTTATA AAATGTAAGT TTTATGAAAA TCTAACAGTA TATCACTGGT TTAATGATCA 3840

CAGCCTAGGA AGAATGGGGA AATTGTCAAA ATCTTCTGTG GATGCACCTG AAGGCCACTG 3900

CTGAACCCAT TTCCCTGCTA GGCACGGCTG CTGGTACCAG GGGCAAACTC CTGGAGTATA 3960

TATGAACCAC CTACATCTCC TTCTCTTCCC CCCCTACCCT TGAGATTTTC ATGTGTCCCT 4020

TAAGGATGTG TGTCCTACTT CCCTTGGAGA GTCACTACCA CATTGAACAC TTTAGACTGT 4080

GAGTCCTGTG AAGATGGGGC TCATGAGTGT ATTGCTCCCC AGTTGTTTCT CTAGCACTAG 4140

CTCAGTATAG GGCATAAAAA TCTGAATGGA TGAACAAACC ACTATTACTG GTGGGGACAT 4200

GCTACTATCT TACATGGTTC GAGGTGGAAT AAAGGTTGAG AACAGCTATA TAATGTGTTC 4260

CTTGAAGGGC AGCAGTACAT CAGTGCAATC AGCCTACCTT CTCCATACTT CTCACTCTGA 4320

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CCAAGCGGGG GGA 18073

(2) INFORMATION FOR SEQ ID NO:13:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7505 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:13:

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CAGTGAAGGA CTAAGGGAAT AGTTAGCCTT CTATTTATTA ACAAATCTTC CCTTTGATGT 660

CTGGATCAGT GTCTCTCTAA TAGGAATTAT TGGCATGTTA AGGCAAAGAA CATATGCTTA 720

TTGAGTGCTG ACTGATTGGG GTTAATACTA ATTTGATACT ATTAAGGTGT GGGGCCCAGG 780

AATGCCAAAA TTCTACCTCA ATGTAGAGCC ACCATTCCCC TTGAGGTAAC CTAGGTGGGA 840

TAGATATACG TGTAAGGGCT AATGGAAGAT AGGGAATCAA AGTATCACTT TATTTTTTAT 900

TTTTATTTTT TATTTAATTT TTTTGAGATG GAGTCTTGCT CTGTTGCTAG GCTGTAGCGC 960

AGTGGCACAA TGAAAGTATC ACTTTATTAT TATCTGAGCT TGTGCCCTAA ACTTCACTGC 1020

AGAATATGCT GGTAAAATGG ACTGGATTAC AGGATTTAGA GGCAAGGTCC ACAGGTCAGG 1080

ATAAGAGGTA AAGAGGGAAA TCTTTCTCTC TTCCTAAGCC CAAACCCTCC ATGACAATTG 1140

AGATTAAAAA AAAAAAATAA ACTGATGAGA GAATCCAAGC ACAGTTGATC AAAGAGGAAA 1200

GAGAAATGAT GATGTTTCCC TCTTTCTTTT TCATGAGAAA GTGGCTCTCT TATTGATCGG 1260

CTACTTGATT AGAGAAACAG TGGGGGAAAG AACTGCCATA TCCACATGTG CAATTTTTTA 1320

AAACACACAG TGATTCTGAA CACTAGTATA AATTCCCAGT CAGTGTTCTG GCCATCTGAC 1380

TACTCAGGTT ATAATACCTA ATTTTTACAA GGGAGTTGGG AAGTGTGCCA AACCTGTAGA 1440

AGTCTATATC TACTGTATTC AGATTTTATA TGCATTATTT TATATAACCT TTTGACCTCT 1500

CTCCTCTATC ATCACTTGAG TGATTTCATC CAGCGTCATC ATTTAACATA TTTTAAATAA 1560

CTCTATATAC TGATAATTCC CAAATTTATA TCTCCATCCC CGATTGTTCT CCTAACCTCC 1620

AGCCTCTAAT ATCCAACTGC CTACTCAAGC CTCAGCAATG GTGAGCGCCC CTGCCCCAGC 1680

CTCGCTGCTG CCTTGCAGCT CGATCTCAGA CTGCTGTGCT GGCAATGAGC GAGGCTCCGT 1740

GGGCGTGGGA CCTTCCGAGC CAGGCGCAGG ATATAATCTC CTGGTGTGCT GTTTGCTAAG 1800

ACCGTTGGAA AAGCACAGTA TTAGGGTGGG AGTGACCCAA TTTTCCAGGT GTCGTCTGTC 1860

ACAGCTTTGC TTGGCTACGA AAGGGAATTC GCTGACCCCT TGCACTTCCT GGGTGAGGCA 1920

ATGCCTCGCC CTGCTTCGGC TCATGCTCAG TGCGCTGCAC CCACTGTCCT GCACCCAGTG 1980

TCCGACGAGC CCCAGTGGGA TGAACCCGGT ACCTCAGTTG GAAATACAGA AATCACCCGT 2040

CTTCTGTGTC CCTCATGCTG GGAGCTGTAG ACTGGAGCTG TTCCTATTTG GCCATCTTGG 2100

AACTGCCTTG CATTCAGTTT TTAATATCCA ACTGCCTATA CGATATCTTC ACTTGGATTT 2160

TGAATAGGCA TATCAAACTT GTCATGTTCA AAAGTGAGGT TCTAATCTTC CCTCCCAAAC 2220

CTGCTTCTCC CATGGCTTTC CCCATCTCAG TAAATAGGAA TTTCATCCTT CCAATTGCTC 2280

ATGCCAAAAA TTTGGGAGTT ATCCTTGACT CTTCTCTTTC TCACACCCCA CATTCAATCC 2340

ATCACCACAT TCTGATGCCT CTATCTTCAA GATATACTTA GACTTTCACC ACTTTTCTTC 2400

ACTCTGCAAT TACCACTTTG GTCCAAGCCA CTGTTATCTC TTTCTTGGAT TATTGTAATA 2460

GCTTCCTAAT AATTTGTCCC CTTTCTTCCA CCTTTGTTTC CCCTACAGTA TAATCTTAAC 2520

GAAGCAGCCA GAATGGTTGC CTACAAACCT TTAAAATGGT AAGCCAGAAC ATGTAGGTAT 2580

ATTCAAAACC TTCCAATGGC TTGTCATGGA ACTAAAAGTC TCTACATTGG CCTATAAGAC 2640

CCTATGTCAT CTACCCCTAG TCTCCTCCTT TCTAACTTCA TCTCCTGCTA TGCTGTCCTT 2700

CAACTCACTC TGCTCCAGGT GCTCTGGCCT CCTCAAACAC ACCACACACA CTTGCAGCTC 2760

ACAGTCTTGG CACTTGCTGT TCTTCTCCTC TAGGACCTTC TTCCTCCAAC TGTCTGGTTC 2820

ACCCACCCCT TCCTTCTGGA TTTCTGCTCT GATGTCATTT TATCAGTGGG CACTTCCCAA 2880

TTTCTCTATT TAAGACCACA ATTCCAGGCC AGGGTGGTGG TTCATGCCTG TAATCCCAGC 2940

ACTTTGGGAA GCCGAGGTGG GCAGATCATG AGGTCAAGAA TTCGAGACCA GCTTGGCCAA 3000

CATGGTGAAA CCCCATCTCT ACTAAAAATA CAAAAAAAAT TAGCCAGGTG TGGTGGCACA 3060

TGCCTGTAAT CTCAGCTACT TAGGAGGCTG AGGCAGGAGA ATCGCTTGAA CCTGGGGGGC 3120

AGAGGTTGTA GTGAGCCGAG ATTGCGCCAC TGCACTTCAG CCTGGGCAAT AGAGCGAGAC 3180

TCTGTCTCAA AAAAAAAAAA AAATTTGCTG TTATTTCCTA TACTATTTTT GTAAGGCAAG 3240

GACCTTATTA TTTTCCTTGA TAATACCTCT CACACTTTAT AATTACATAT TTGACTTTGT 3300

TGATTAATGA ATATCCCTCC TTTATAGCAT AAATTCCACA AGAGCAAGGA TTACATGTCT 3360

GCTTCATTCT CACTGTACAC CTAAAACCTA GCACAGGGTC TCACACATAA CAGGCACAAA 3420

ACAAACAATG GATTACGTTG AGCCAAAGAA CAAAAAAAAA TAGTAATTTA TCACTAAATG 3480

TCTTTGTTAA ATTCCAACAA CAGGGGGCAG TATATCAGGT ATTATAAGAA AGTAATTAGG 3540

CACATCCCAG CACTTTGGGA GGCCGAGGCG GGTGGATCAC AAGGTCAGGA GTTCAAGACC 3600

AGCCTGGCCA ATATGGTGAA ACCCCGTCTC TGCTAAAAAT ACAAAATTAG CGGGTGTGGT 3660

GGCACACCCC TCTGGTCCCA GCTACTCAGG AGGCTGAGGC AGGAGAATCG CTTGTACCCA 3720

GGAGGCGGAG GTTTCAGTGA GCCAAGATCG TGCCACTGCA CTCCAGCCTG GGTGACGGAG 3780

CGAGACTCTG CCTCAAAAAA AAAAAAAAAA AGAAGAAGAA GAAAGTAATT AGGCACCTTT 3840

GGCTTAAGAC ACTGGGCTAA ATCCATGAAT TTACTTCATC TTCCCCCAAA GCACACTGAC 3900

ATGGTAGAAG AAATATAAAA ATACTAATGA ATCAACAGCA TATCTGAAAG GCAGCAAACG 3960

GTGGCATATG TAGATCAGAA TCTTTGAGAG ATTTCTGGAA GACAAAACAG ACCAGACTCG 4020

ATGTCCAAGA GATCAAACAG AGCCAAAGAG CCTCCAGCTG AAAACTAAGT ACTAGTTCTA 4080

CCAGTTTGGG CCTGGAAACA CCTCAAGCTC AGAGGGAATT GGGACTGGGG TTGAAAGTGG 4140

ACCTTGAGGT ACCAGGATGG TACTTAAGCA AAGGCCTGCC AACCCAGCAC CAGTACACCC 4200

ACAGCCCAAA TGACAAGCGG GGCTTCCCAT CTAGACTCAG CTGGAAAAAC AGTGCTCTAC 4260

ACAGAGTAGA GAGTTTGTCA CAGAGACTGG TAAGGGCTTC TTTTTTACAA AACATATGCT 4320

GCATATATAT TTTCTCAACG TCACACTAAT GACATTTTGG GCTATACAAT TCTCTGTTAT 4380

GTGGGTCTGT CATGTGCACT GTAGGACATT TAACAATATC CCTAGCCTCT AATTATTAGA 4440

TGTCTGTAGC AAATTCCCAA TTTTGATGAC CAAAAGTATC TCCAAGCATT GCTAAATGCC 4500

TTTGTGGGGG AAATAGCCCC CAGTAAGGAA CCACTGGTCT ATACTCACGC CATTCTAACT 4560

GAATTCTTTT AAGGCAAATC CGAGACCTAG CATTTCAAAT GCAATTACTT AGGTATGTAT 4620

CACCAAGAGA TCAAGATTCT TAACATAAAC ATAATACTAT TATCCAATTT AAAAAGTAAC 4680

ACTAATTCCT TAGTATCATC TAATATTATT CAGTTACTGC TTGAATTTCC CTGAGTGTCT 4740

CATAAATGCT TTTTTTTTGT TTTGGTTAGA ATTGACACCA GAGCAGGTCT ACACTGCATA 4800

TGATTGTTAA GTATATTGGG TCCACAGAAG GTCTCCTGGG GCCTGCAGAC AGAAAAAAAC 4860

CATAGTAGTG CCCAAGCTAA TTCTAGGCAA CCACAAGAGA GGAAAGGAAA AAGAAAACGG 4920

CAGCTCGCCT AGAGGATAAC TGCACCCTGC CCCGATTTTC CTGAGCCATC ACTGAACCCC 4980

TTCCTGGTTT AGGACGTATG TCCATGTTTG TCTTCTGAAG GGATGAAGGG ACACCTATTG 5040

TGAGCACAGT CTAAGCCACT CAATGGTCCA GGGCATAGCT CAAACAGAGC AACAGTAGCC 5100

CTGGGAAATG GAGGTGACAA AAGAAACAGA ATAAATCTTT CAAAATATAC TGCAATTTGT 5160

GCAACAGGAT GCCATATTGA TTTAAAAAAA TTTTTTTTCT TAAATTTTTT GTAGAGATGG 5220

GGGGAGGGGG TCTTGTTGTT GCCCAGGCTG GTCTTGAACT CTTGGTCTCA AGTGATCTTC 5280

TTGCCTTGGC CTCCCAAAAT GCTATGATTA TGTGCGTGAG CCACTGCTGC ATTGCGTTTT 5340

TTTTTCTTTT CTCGAGACGG AGTCTCACTC CGTCACCCAG GCTGAAGTGC ACTGGCGTGA 5400

TCTTGGTTCA CTGCAACGGC CTCCTGGTTC GAGCGATCCT CACACCTTAG CCTCCCTAGT 5460

AGCTGGAACT GCAGGCCTGG CTAAGTTTTG TATTTTTAGT AGAGACAGGG TTTCACTATG 5520

TTGGCCAGCC TGGTCTTGAA CTCCTGACCT CAGGTGATCA GCCTGCCTCA GCCTCCCAAA 5580

GTGCTGGGAT TATAGGTGTG AGCCACTGTG CCCAGCCTAC ATTGATATTT TTTAAAAGCC 5640

ACTATTTAAA AAGGAGTAAT CTGAGTAGTA AGAAGGAGTT CTTTAAAAAC TGGCCGGGCA 5700

TGGTGGCTCA CGCCTGTAAT CCCAACACTT TGGGAGGCCG AGGCAGGCAG ATCACCTGAG 5760

GTTGGTAGTT TAAGAGCAGC CTGACCAACA TAGAGAAACC CCATCTCTAC TAAAAATACA 5820

AAATTAGCCA GGTGTGGTGG CACATGCCTG TAATCCCAGC TACTCTGGGG GCTGAGGCAG 5880

GAGAATCGTT TGAACCTGGA AGGCAGAGGT TGCGGTGAAC CGAGATCGTG CCATTGCACA 5940

CCAGCTTGGG CAACAAGAGC AAAACTCCGT CTCAAAACAA AACAAAACAA AAATGAAAAC 6000

AAACAAAAAA ACACCAACAT GATTAGGAGG GAAAAAATCT AGATAGAAAG GCTTAACAGG 6060

GCCGGGCACG GTGGCTCATG CCTGTAAGCC CAACACTTTG GGAGGCCAGG GTGGGAGGAC 6120

TGCTTGAGGC CAGGAGTTTG AGACCAGCCT GGGCAACTTA GCGAGACTCT GGTAGTCTGT 6180

CTCTACCAAA CAAACAAACA AACACCTGAT TAGCTGGGCA TGGTGGCATA TGCCTATAGT 6240

CCCAGCTACC CGGGAGGCTG AGGCTGGAGG ATCGCTTGAG TCCCAGAGGT CAAGGCTGCA 6300

GTGAGCTGTG ATCAGGCCAC TGCACTCCAG CCTGGGCGAC AGAGCATGAG TCTGCCCCAG 6360

CCCTGCCTCC AAAAAAAGAA AGGCTAAATA GGAGAACTGA TATAACTGAA AACCAAATTA 6420

GTTGTGTGAA AGAGCAACTG TCCTGGAAGC TCCCAGAACA CAGAGCAATA AGAGATGAAA 6480

AATATGACAG CATAGAAAAG AAAGGAACTG GATAGGTCCA GGAGATCCAA TACCTGTGCA 6540

ACAGGAGAGT CCAAAGAAGA AACCAGTAAG AAGGGAGAGA AGTAATACAA GAAAGTTCCT 6600

GAGTTATCAG GCCAAAAGAA ATAATCTAGT TTGTGGAGTA ATATTGACAA AAAAATCTTT 6660

ACACCTAGAT GTATTCTGAA AAAATTCTTA AATTCTAATT GAAATCAACC AACGAACCAC 6720

AGGCCAGCCT TAGAAAACCA TTTCCAGGGC ATGGGGTTTT AGGGTCTGAC AGACCTGAAG 6780

TTCAAATTCC TACTATCCTA ACTTACTAGT AGTGTGATAA TCTCTTAGAA CAATGTATGA 6840

AATGGAAGCA TAATAGCACC CTCCACCTTT TAGAGTTAAT GGGAGATCTA AAAGAGGTAA 6900

CATTTGCAAA GTGTCTGACA TGAAGGGAAG AGATTGGCTT TGGCATCCAC AAGTTCACAC 6960

ACTAGCAGAG AACCTCAGTC CAGCTTCCTA CGCTCAGGCA GTTCTTTGCC TAGAAGAGGG 7020

GTCGGCAAAC TATAGCCCAA ATTTAGCCCA CTGCCTGTTT TTGTAAATAA AATGCTATCA 7080

GAACATGGCC ATGTTCATTC ATTTACATAC CATCTATGGC TGCTTTTACA TTACAAAGGC 7140

AGAGCTGAGT AGATGAGACA GAGACAGTAT GGTTACAAAC CGAAACTGTT TCAACCCCAA 7200

CTTCATTCCA GCAAAGTTTT ACTTTCTAGA TTCAGGCCAG GGAGCAAGCA TGAAAATGAA 7260

AACCACTAAA ATGGTGTCCC GGGACAACAG ATACCTACTT GCTATAACTT CTTTCCTTGA 7320

AAACAAAGGG CCATATTAAT TGAAGGGCTC ACCTCTAAAC AGGTGAGTGA CTTAAGGACT 7380

TCAGACACAC ACTGGTCAAC TACAAACTAG TCAGTAAAGG AATAGCCATA GTCCTATAGC 7440

CCCAGTTCCT ATGGCCCAGG GGGATCCACT AGTTCTAGAG CGGCCGCCAC CGCGGTGGAC 7500

TCCAG 7505

(2) INFORMATION FOR SEQ ID NO:14:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 529 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:

GCTGAGGTGC ATCGCGGTGG CGGACGCTCT AGAACTAGTG GATCCCCAAA CAAAACCTGT 60

CCCTGCTAAT GATGGTAGAC CCAATCAGAT CCCCGGAGAA GCCGAAATAC GGAAACCATA 120

TCAGCATACG CATGGCATAC ATAGAACCCC ATACATGGAT TGCTTACTCA GCCAGATATA 180

GAAATCTATC TTCACGATAG AGATATATAT ATATAGACAC ACTGCATATA CAGATGTGAG 240

ATGGAGGCTC ACTCTGCCAC CCGTGCTGGA TCTACAGTGG CACAAGCTCA GTCCACAGTC 300

ACGTCGATCT GCCGGGCGTG ACCGACTGAG ATGCAGCGGC CTCGGGCGTA GCTGTGAGTA 360

CACGCACCAG TCATCGCGAC TGGCTGCAAG TGGTATAAGC GGAGGGGACA GGGTTACAGC 420

ATGACGGCTA GGCAGGCCGC AAACTGAGGA CCACAAGAGT GCCACGCTGC CCGAACGCAT 480

GCAGTGGCGA GATTACATGG GGCAGCCACT AGAGCCGCCG TATCAGAAA 529

(2) INFORMATION FOR SEQ ID NO:15:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 635 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:

TACCACGCGG TAGCGCCGCT CTAGAACTAG TGGATCGGGT AATCCAGCAC TTTGGGAGGC 60

CAAGGAGGGC AGATCACCTG AAGTCAGGAG TTTGAGACCA GCCTGGCCAA CATGGTGAAA 120

CTCCATCTCT ACTAAAATTA CAAAAATTAG CCGGGCGTGG TGGCGCATGC CTGTAATCCC 180

AGCTACTCGA GAGGCTGCGG CATGACAGTC ACTCAAGCCC GGGAGGTAGA GGTTGCAGTG 240

AGCTGAGATT GTGCCACTGC ACTCCAGCCT GGGTGGCAGA GTGAGACCCT GTCTAAAAAA 300

AAAAAAAAAA AAAGGCCCAT TAGGGGACCC AAACGGTTCC CCAGCTTTGT TGGATTTCCC 360

CAAATTTGGG GCCAATTTTT GGAGGGTTGT CCCTTAAAAA TTTAAATTTG GGGGTTTTTT 420

TCCAGGCGCC CATTAGAAAT GGGTTCCGAA AATTTTTTGG CCAAAAAAAT TTGGTTTAAC 480

CGCGGACCAA AATCCTAAGG TTTAACTTTT TCCTAAACCT TTTAGAATTT AAAGTTTCCG 540

GGGTTTCTCA GGAGGGGGTA ACCCTTCACC CCAATATAAC TCGGAAACCC CCCTTTTTTA 600

GGAAAAGGGG AATTAGTGGT GCTTTCCGGG CCAAA 635

(2) INFORMATION FOR SEQ ID NO:16:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 938 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:16:

CCCAGGGACC AAGCGAGTGC GACCGCTCTA GAACTAGTGG ATCCCCCTTG AAGACTATAT 60

TTCTTTTCAT CACGTGCTAT AAAAATAATT ATAATTTAAA TTTTTTAATA TAAATATATA 120

AATTAAAAAT AGAAAGTAAA AAAAGAAATT AAAGAAAAAA TAGTTTTTGG TTTCCGAAGA 180

TGTATAATAG GTTGAAAGTT AGAAATTATT ATTATAATAG CAAAAAAAAT TTAAAGTTAG 240

AAATTAGAAT TTAAGGCTCT ACACACGTTT ACGATGATAT TGGACGAACG ACACGATTAG 300

ACAGTTGTAG GTTGTGTGTT GTGATGTTTT TGAGTGATTT GTAGTGTTTA ACCTTGTGGT 360

TTGGAAAGGT NGTATGAGTA TTAATCTCGG GCTTATTGGG AGGTTTATGT GCAATGCATT 420

TTGTGGTTTT TTTATAATGT TGTGTTTAGG GTTAAAACCT GTTGTGTATA TTGTGTTGGT 480

TTGTTGCTTG TTTGTACATT GGTATGATGC CTNTTTTGCT TATGGGTTNG GTGTTTGGTT 540

TTGGTTGTGT TTTTTGTGGT GTGTTGTTTG ATAGTTTTAG CGGTTGTTTT TGGGTTGTTG 600

TTTTATGTTG TGGTGGTGTT TTGTGTGTAG AGTTGTGGTT TGTGTGTTTT GTTGGTTGTG 660

TTGTGGTATT GTTTATGTTT GTCGTGTGTA TGGTTTGTTG TTAGTCGTTG TTGTAGGCTT 720

GTGTGTTGTG TGTTGTGTGT GCGTGTGGTC TAGTTTGGGT GGTATTGTTG ATTTAGTGTG 780

ATAGTCTGTT AGAGTTTGGG TTGTTGTGTG TATTGGGTTT GTCTGTGTGT GGTTTTTTTG 840

TGGGTGTAGA TGATGATTTG TGTATGTGGG TGAGGTATAT GTTATTTGTG GTATTTCGGT 900

TGTGATGTGT TGGTTATTAT GTGTTTGTTA TGTGTATT 938

(2) INFORMATION FOR SEQ ID NO:17:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1145 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:17:

GTCTCCGAGC TCACCGCGGT GGCGGCCGCT CTAGAACTAG TGGATCCCCC GCTCTCACTC 60

CCTGACTCTT GCCTTCTGTA ACAACTGGAG ACAACTCTTT CAAAACCAGC TCCAAGCCCC 120

AGACTTCTCT CTGGGCTTTA GTTCGTAAGG CAGGTGCCCT ACTGAGTGAG CCTAGATCAG 180

ACAGAAACAT AGCTGTTGGC AAGGATTTAG GTGAATTTCC TTCCATTGTT TTTCTAATAC 240

CTTTTTTTTT TTTTGGAAAA TATAACCATG CACCTACACA CATATTTGAA TATCCTGCCT 300

TTTTATTTAA AATGACATGA TAGGTCCGGG AGTGGTGGCT CATGCCTGTA ATCCCAGCAC 360

TTTGGGAGGC CGAGGTGGGC AGATCACCTG AGGTCAGGAG TTCGAGACCA GCCTGGCCAA 420

CATGGTGAAA CTCCATCTCT ACTAAAAATC AAAAATTAGC CGGGCATGGT GGCAGGCTCC 480

CAGCTACTCA GGAGGCTGAG ATGTGAAAAT CGCTTGAACC CGGGAGGTAG AGGTTGCAGT 540

GAGCTGAGAT CTTGCCATTG CACTCCAGCC TGGGCAATAA GAGCGAAACT CCATCTCAAA 600

AAAAAAAAAA AAAACCCAGG GATAAACTTT CCAAAAGGCC CCAAAAAGGG GCATGATTAA 660

GACAATAAAT TAGTCGAAAA TTGTCAATAT AAATGAATAA TAATTTTTTT GGCCATTCTG 720

CCAAGTGGCA TAACCCTGTC ATTCTGCCCA TTCGGCAACT CTTTTTCCTC CCGGGGAATC 780

GCTCCCACTT TTTGCATGGG TTTTGGATGG AACTGTTGGT CACAGGTTTT TCACCCCCAT 840

TTGGCCCTCC CAGAGGTGTA CAAAGTACCC CAGCCTGGCC CTTTTTCACC CAATTTTCCC 900

AGGTATATTC CCCCGGTTTT GGTCCCAGGT TTTAACCCCC CCCTCCAAAG GGCTTTGGGT 960

TTTGGAAGGA TTAAGTCCTC GAAATAGGCC CCTCATAATA CCTGGGGGGG GGACCTTTTT 1020

CAAAGTTGTG GGCACCTCTT GTGTCGCCCC CACGGGGGAC TGATGTATTT ACGCCCCNTT 1080

GGGGNNTAAT ATGGATTGNT ATGTATTGGG CGAGGAGAAA ATATTTTTGA TGGGGTTTTT 1140

CTCTT 1145

(2) INFORMATION FOR SEQ ID NO:18:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 852 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:18:

TCACCGCGGT GGCGGCCGCT CTAGAACTAG TGGATCCCCC GTTTTGCTCT CTCCTTAGAA 60

TGAGCTGGGA ACTAGTCACT CTTGTTTTCT CACCTATAAT AGCATCTGGG TCCAGTGTTT 120

TTTATGTGGG ACAAATTTGA ACTTGTGGTC AACCTCTTTA ATTGTAAGAA TATTCAGGTC 180

TTTTGTTCTT CCTGGGCTAG TTTTTTATTC TTTTTCTAGA GATTCGTTCA TTTTTCTTAG 240

TTTTATTTGC CTATAATTGT GGATAATCTG TTTTTTATCT GCTACTTCTG TAATTATTTC 300

CACATTTGAT TTATAATATT AACTTGTGGG CCAGGCGTCG TGGCTCACAC CTGTAATCCC 360

AGCACTTTGG GAGGCCGAGG CGGGCGGATC ACGAGGTCAA GAGATTGAGG TGAAACCCCC 420

TCTCTACTAA AAGTAGAAAA ATTAGCTGGG CATGGTGGTG CGTGCCTGTA ATCCCAGCTA 480

CTCAGGAGAC TGAGGCAGGG AATCTCTTGA ACCCAGGAGG CAGAGGTTGC GGTGAGCCAA 540

GATTGCACCA CGGCACTCCA GCCTGGTGAC AGAGCGAGAC TCCATCTCAA AAAAAGAAAA 600

AAAAAAAACT GTCAAATGAT ACTCCAAAAT GGTTGTACCA TTTTATATTT GCAACAACAA 660

TGTCTGAGGG TACTGATTGC TCCATATCCT TGACAGCACT TGGTATAGCC GATCCTTTAA 720

TTTTAGGCAC TTTAAGGGGG CAAATACCTG GGATTTTAAA GGTTTAACCT TTTTATTTTC 780

CCAAATGGGT TAATAGGTTC TCAGCAACTT TTCAAGGGGC CTAATTCCCC CCTTCAAAAT 840

AACCTCCCCT GG 852

(2) INFORMATION FOR SEQ ID NO:19:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1854 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:

CCGGCACTCA CCGCGGTGGC GGCCGCTCTA GAACTAGTGG ATCCCCGGAA ATGTTACTTC 60

CAACATTTTA GAACTGAAAT GATTCTTAGT CTGGTGATAA ATGTCAATTA AAATAGTTCT 120

CCTTTCACAG AGAAAATTAA GAAAAAATTA GTTCAAGAAA ATATCAATCA TGATTGCCAG 180

CGGAAATTTG TTTCTGCAGT AAAACAAGCA AAACAAATCA AATCCATTAA AACTAGCAAC 240

AGACTGTCTT CTAAAGTCAA GTTCACATCT GGAGATTTTT ATAAACTTTA TTGGAAAAGT 300

TCTGGTTATC TATATTTTTA GCATAGCAAA ATATTCTTCT TGTTTGTTGA ATTTGATATA 360

AAATGTTATT TTTAGCCAAG TCCTGGGGCA ACTCCTACAT GGCTGGAAAA TGTTCTCGGT 420

GTTAACAAAG ATGCAAAGAT CTTAAATATT AATGTTATCA ATCAACTGGA TACTCTTAAG 480

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TATTATTTGT AATTATGTCC AATGTCATCA CCACAGGGCT GACCAACAAG CAAAGAGCTG     540
ACAGTAGTAG CAAAATGTAG AAATCTCTGG TAAGCATGTT GTGTTTATCA ATCCTCTTCA     600
AATAGATGAA ATTAAATTGC ATTTAAAGAA TGTTACTTAT ATTAGGCATT TTTTGTGAAA     660
GACGTTTTAA ACTATGGTGT CAGAAAACAG AAATACTAAA CAGAATGCAT TTAACAGGAC     720
CTTGAAATCA CTGAATACTC ACCTGTGTAA AAGTCAAAGT TCAGATAATT GAAATGTTCT     780
TACTAGTCTC AAGATGTCTT TTGGTTACAT AGAAATTTCC ATGCTGAATT TTGATTTTTT     840
TAAAAAGCCA TTAATATGAG TCAAAATCCA TTATTTCACA AGTAAATGAC CTTTTTATTA     900
AAAAAAAAAA AGAGAGAGAG AGAAGAGCAA GGAACCACCC ACATCTAACC TCTTAAATCT     960
GAGATCAATA TATCAAAATT TTAATGTACA TTGAAAACAT TTTCATTTTA TTCCACACAC    1020
TACCTTTTCT TCATAATTTC TTATTCTGGA CATATAGCAG TTTTTTTTGT CTTTTAAAAC    1080
AGGAAAAATA AACAAACATG GTCTTATTAT TGTTACTAAG TCACAGGTAG TAAAGATGGG    1140
ACCAGGAGAA CCTTGGAGGA CTAGAAACTT CTCAAGAGTA GTTAGATTTC ACATTCAGAG    1200
GGAGGACTCA GAGTCCTGCC TGGGACATAC ATTTGCATTC TAGGCTCAAG AGCAAATATG    1260
TCAGCTTTCC TTTGGTCAAA CAATCTTTGC TACAGGTCCT AGGTAGTTAT ATCAGTGGAA    1320
CCTACTAAAG ATGATGGAAT TTGTGGTATT TCAGGGTAGG AGGTAAAGTC TTAGCAGGCT    1380
CAACTATACA TGATCTTAAA ACTAAATTTG AAATGCAGAT GTTCTATGAG TTAGTTGGAT    1440
ATTGTAGTTA TCCCATCTAT CAACTGATCA CATTTGGTAT GAGCTTGTTA GTTCTGATTA    1500
GGACTCATCT CAACATAATA AGAAGGGTGG CATTTAGGGC CCAGTGTGGG GGCCTAGTGA    1560
TCACTGCTGG GACACTGCTT CTAAATCAAC ATAACTAACC TCTCTAGGAT GGCAGGCTGA    1620
GGCTGCTCAA GTACTTCCTG TCTGGCATCT GGGACAGGGC TGAGTCTCTG GGTGGGAAGA    1680
TGGGTGGGAG GACTGAGGCT GATGAGTATA TGATATAAAT GAGAGCCATT GGAATGGCTC    1740
CACATACAGG ACATGTTGAT AAATCATTTT AACATATTTT GCTTTCTCTC TCTGGTGGCC    1800
CATTGAGAAT CAAAAGGGGG ATCCACTAGT TCTAGAGCGG CCGCCACCGC GGTA          1854
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(2) INFORMATION FOR SEQ ID NO:20:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1101 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:20:

CCACCTTTTC AATTCATCAT TTTTTTTTTA TTCTTTTTTT TGATTTCGGT TTCCTTGAAA 60

TTTTTTTGAT TCGGTAATCT CCGAACAGAA GGAAGAACGA AGGAAGGAGC ACAGACTTAG 120

ATTGGTATAT ATACGCATAT GTAGTGTTGA AGAAACATGA AATTGCCCAG TATTCTTAAC 180

CCAACTGCAC AGAACAAAAA CCTGCAGGAA ACGAAGATAA ATCATGTCGA AAGCTACATA 240

TAAGGAACGT GCTGCTACTC ATCCTAGTCC TGTTGCTGCC AAGCTATTTA ATATCATGCA 300

CGAAAAGCAA ACAAACTTGT GTGCTTCATT GGATGTTCGT ACCACCAAGG AATTACTGGA 360

GTTAGTTGAA GCATTAGGTC CCAAAATTTG TTTACTAAAA ACACATGTGG ATATCTTGAC 420

TGATTTTTCC ATGGAGGGCA CAGTTAAGCC GCTAAAGGCA TTATCCGCCA AGTACAATTT 480

TTTACTCTTC GAAGACAGAA AATTTGCTGA CATTGGTAAT ACAGTCAAAT TGCAGTACTC 540

TGCGGGTGTA TACAGAATAG CAGAATGGGC AGACATTACG AATGCACACG GTGTGGTGGG 600

CCCAGGTATT GTTAGCGGTT TGAAGCAGGC GGCAGAAGAA GTAACAAAGG AACCTAGAGG 660

CCTTTTGATG TTAGCAGAAT TGTCATGCAA GGGCTCCCTA TCTACTGGAG AATATACTAA 720

GGGTACTGTT GACATTGCGA AGAGCGACAA AGATTTTGTT ATCGGCTTTA TTGCTCAAAG 780

AGACATGGGT GGAAGAGATG AAGGTTACGA TTGGTTGATT ATGACACCCG GTGTGGGTTT 840

AGATGACAAG GGAGACGCAT TGGGTCAACA GTATAGAACC GTGGATGATG TGGTCTCTAC 900

AGGATCTGAC ATTATTATTG TTGGAAGAGG ACTATTTGCA AAGGGAAGGG ATGCTAAGGT 960

AGAGGGTGAA CGTTACAGAA AAGCAGGCTG GGAAGCATAT TTGAGAAGAT GCGGCCAGCA 1020

AAACTAAAAA ACTGTATTAT AAGTAAATGC ATGTATACTA AACTCACAAA TTAGAGCTTC 1080

AATTTAATTA TATCAGTTAT T 1101

(2) INFORMATION FOR SEQ ID NO:21:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 120 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:21:

AACTAATGTA TCCCCCGGGC TGCAGGAACA CGATATAAAG CCTTAAAATT GTGCGAATGT 60

GRTAAGTCGA TCCAATCTCA ACTGCTATCT RTGTACCAGA ATAGTTTCAT AATTACGTGT 120

(2) INFORMATION FOR SEQ ID NO:22:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 300 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:22:

GAATTCTCTG WKATTAKAAC TATCTTGMCT CAAATTSACT TGGTGAGCTA ACCTGGCCTG 60

TGGTCCCTTG GCTTTAATGG AGGCTTTGTC ATATAGATCA TMTGTGGTAC TKGTGCCTAG 120

TTGTAGTGCC CTGCCTTGCT STTCTWGGCT TACTKGATTT WGGGGTATAC ATCWATKTAA 180

YTSAAAGGTC TTTCTCCTCC CGYYGGGAGA ATTTCTCCTC CTCCCTCGGA GAACTCTTTC 240

TSCCGAAATT CTATTCCGGG CTGGGTCTCC ATTCTGCTTA CCTCCCACAC TTTTAATMAA 300

(2) INFORMATION FOR SEQ ID NO:23:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 599 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:23:

GAATTCCCTC TTGCTTGGGG GAGGTCAGCC TTTTGTTCTA TTCAAATCTT TGAGGAAAAT 60

AGAAAGCAAA GAATATATTA ACTATATTAA ACAAACTAAA TGTTCCAATT AAAATACAAA 120

AATTATAAAG CCTAATAATA AAAGCCCTCA ATTATATGCT GTTTAAAAGA GACATTTTTA 180

AGCTTAAGGA TATAGAAAAG TTGAAAATAA AAGAATGGAA TAAAATAAGC CATGAAAATA 240

CTAGTATAAC ACTGATGTCA AAATCTGACA AAGCACACAA AAAAGAAAAT AACTTTAACT 300

GCAAAATCTT AAAATCCTAG CAAAGAAAAA GCAGCATATG TTATAATTAT ACCACAACCT 360

GATCAAGTAA GGCTTACTTC AAAAATTTAA CCATGGTCCA TTATTGGAAA ACATATTAAT 420

AAAAATCCTC ACAAAAATAA TTCAAAATAT AAAAAGCCAT ATGATAAGCC TGATGAATGC 480

TGGTTTACAG AACTGGTTTT CTTTAAAAAG GCAATCATTG GGGAAATAAC CCGCTTACTC 540

AGTATTTACT ATGTGCTAGC CCTGTTCCTT CTACTAGAAA TTAGTGAACA AATTCTAAC 599

(2) INFORMATION FOR SEQ ID NO:24:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 330 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:24:

AAGCTTTCAA GAACAGGGAC TGTTAAGCCG GGTACAGTGG CTCACACCTA TAATCCTAGC 60

ATTTTGGGAG GCCAAGGCGG GTGGATCACT TGAGGTCAGG AGTTCAAGAC CAGCCTGGCC 120

AACATGGTGA AACCCCATCT CTACTAAAAA AAAAAAAAAA AAAAAAAAAA AAAGAAATWC 180

MAAAATTACC CAGGCATGGT GGCACGCGCC TGTAATCCCA KCTACTTGGG AGGCTGAGGC 240

AGGAAAATTG CTTGAACCTA GGAGGCGGAG GTGGCAGTGA CCTAATCACA CCACTGTTCT 300

CCATCCTGGG CAACAGAACG AAACTGTTTC 330

(2) INFORMATION FOR SEQ ID NO:25:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 258 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:25:

AAGCTTGGGT GATAATGAGG AGTCAATGTT GGTCCATCAA TTGCAACAAA GGTACCACAG 60

TGGTGTAGGA TGTGGATAAT GAGGAGGCTG TGCACGTGTT GGGGACAGGT GGTATTTACG 120

AATGCTCTAT ATTTTCTTTC TCTCTTTTTT TAGGACGGAG TCTCACTCTG TTGCCCACGC 180

TGGAATGCAY GGGCATGACT GTGGCTCACT GTACCCCCCA CTCCCCATGT TCAAGAGATT 240

CTCTTGCCTC ACCTCCTG 258

(2) INFORMATION FOR SEQ ID NO:26:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 622 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:26:

CTCGAGTCCA CCGCGGTGGC GGCCGCTCTA GAACTAGTGG ATCCCCCGAT TTATTTAAAG 60

CAGTTATGTA TGTATGAAAA ACAATGCTGA GCATTCAATT CCAAGATTTC TGAAGACACC 120

TATTTTACCA TCACTTTGAA TAAAATTTTT ATATTCCTTT CTTCAAATAC CATCTCGGTT 180

TTCAAATGTG GCTCATTAAA TGTGAAAGCA AAATTTCATT TCAAATAGCA GCCTTATCAA 240

ATGACAATTT ACCTGTGGTA GCATTGTTGG CACTGACACA TATCAGACCA CTGCCGAGCA 300

GAACAAGAAT GAACCAGGAA TCCATGCTTA TCTGGAAAAT AGGGAGTCAT GTTAGATGAG 360

GTCCTATATT ATCAGGACTA TGTCTGAGCT GGTCACCAGA AGAGTATTCT GGATTTCCAA 420

GCTATTAAAA TGTGTGCCTA AACCAATGAT CTTTTGGGAG CCTGATATGC ATGCTTCCTC 480

AGATATCCAA TAACTAATTG AGTCTTTATA AAGACTGACT ATCCCTTATC TTGAGGACTA 540

GCAGTGTTTC AGATTTTTTT TAAGAGATAG GGTCTTGCTC TGTTGCCAGG ATGGAGACAG 600

TGGTTATGAT CATAGCTCAG TG 622

(2) INFORMATION FOR SEQ ID NO:27:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 602 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:27:

TCGGACTCCA CCGCGGTGGC GGCCGCTCTA GAACTAGTGG ATCCCCCGGG CCCTCAGGAC 60

TGCTGGGCTG CCTGGTGTCA GCACTTCCCG CCATTTTCTA TAGCACCAGT ATTATTCTTA 120

ATACTTTAAA AAACCACCAG GCACGGTGGC TCACGCCTGG AATCCCAGCA CTTTGGGAGG 180

CCAAGGTGGG CGGATCACAA GGTCAGGAGA TCAAGACCAT CCTGGCTAAC ACGGTGAAAC 240

CCTGTCTGTA CTAAAAATAG AAAAAAATTA GCTGGGCGTG GTGGCATGCA CCTGTAGTCC 300

CAGCTGCTGG GGAGGCTGAG GCAGGAGAAT GGCGTGAACC CGGGAGGCGG ACTTGCAGTG 360

AGCCGAGATT GCACCACTGC ACTCCAGCCT GGGTGACAGA GCGAGACCCC GTCTCAAAAA 420

AAAAAAGTAA ATAAAAATAA AAAACCATAT CCCACTATCT CCCCCTTCTC TCTTTGCCTG 480

TGACTANNNG GCATACTTAT GGGGAAATCT TTAAGATGTC AGATTTCAGT TCTCTCACTT 540

TTCTACAACT TCTCCCCATT TTGCCTTTCT TAGGAACTTC CCTTCTTCCC ATCTGATTCC 600

TN 602

(2) INFORMATION FOR SEQ ID NO:28:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 546 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:28:

TATCAAGGCG GAGTCCACGG TGGCGGCCGC TCTAGAACTA GTGGATCCCC GAACCAGGAA 60

TCCATGCTTA TCTGGAAAAT AGGGAGTCAT GTTAGATGAG GTCCTATATT ATCAGGACTA 120

TGTCTGAGCT GGTCACCAGA AGAGTATTCT GGATTTCCAA GCTATTAAAA TGTGTGCCTA 180

AACCAATGAT CTTTTGGGAG CCTGATATGC ATGCTTCCTC AGATATCCAA TAACTAATTG 240

AGTCTTTATA AAGACTGACT ATCCCTTATC TTGAGGACTA GCAGTGTTTC AGATTTTTTT 300

TAAGAGATAG GGTCTTGCTC TGTTGCCCAG GATGGAGACA GTGGTTATGA TCATAGCTCA 360

GTGCAGCCTC TACCTCCTGG ACTCAAGTGA TCCTTCTGTC TCAGCCTCCT GAGTAGCTGG 420

GACTATAGGC ATGTACTACG ATGCCTGGCT AATTTTTAAA ATTTTCTGTA GAGACGGCGT 480

CTCACTATGT TGTCTAGGCT GCTCTCAAAC TCTTGGGTTC AACTGATCTC TTGCTTCAAC 540

TTCCAG 546

(2) INFORMATION FOR SEQ ID NO:29:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 498 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:29:

GTGGATTCAG ACGCGGTGGC GGCCGCTCTA GAACTAGTGG ATCCCCCGAG CAGAGGTTGC 60

AGTGAGCCAA GATCGTGCTA CTGTACTCCA GCCTGGGCAA CAGAGCAAGA CTCCGTCTCA 120

AAAAAAAAAA CAAACAAACG ATGTGTGCCT GTGTTTCCTC ATCTGTAGTA TGAGGATAAT 180

GATCATATAT ATTTACTAGT GTTGTTGGGA TGATCAAATT AGGTATATTT AATCATTGTG 240

TAAAAAAGTT GACGTGTAAA ATCCATGTAA AAAAGTTGGC AGAAGAGACA AACTGGTAAA 300

GCAGCCGTTC TTCATTTCTC ATTTCATTCA ACAAGCATTA TTAACAGCCT AGCAAGAACA 360

CAGTATCCAG GAAAAATCAA AGATTATCAA GCTCATGTTC TATAATCAAG CAATTTATAA 420

ACTAGCAGAA GAACAAGACA GATGAATAAG AACTTGGGTA TATTTAAATG CTAAGAAGTT 480

CAATTCAAAT AAATGTCC 498

CLAIMS:

1. An isolated nucleic acid molecule comprising a sequence of nucleotides derived from a eukaryotic chromosome and encompassing a neocentromere or a functional derivative synthetic or hybrid form thereof which nucleic acid molecule or its derivatives, synthetic forms or hybrid forms when introduced into a compatible cell is capable of replicating, acting as an extra-chromosomal element and segregating with cell division.

2. An isolated nucleic acid molecule according to claim 1 wherein the eukaryotic chromosome is a mammalian chromosome.

3. An isolated nucleic acid molecule according to claim 3 wherein the chromosome is a human chromosome.

4. An isolated nucleic acid molecule according to claim 2 wherein the nucleic acid molecule is capable of associating with centromeric binding proteins (CENP)-A and -C or antibodies thereto.

5. An isolated nucleic acid molecule according to claim 4 wherein the chromosome is human chromosome 10 or a modified form of human chromosome 10 or its non-human mammalian or non-mammalian equivalent.

6. An isolated nucleic acid molecule according to claim 5 wherein the nucleotide sequence corresponds to a region mapping between q24 and q26 on chromosome 10.

7. An isolated nucleic acid molecule according to claim 5 wherein a modified form of human chromosome 10 is a mardel (10) chromosome.

8. An isolated nucleic acid molecule according to claim 6 comprising a nucleotide sequence substantially as set forth in SEQ ID NO: 3 or a nucleotide sequence having at least 40% similarity thereto or a nucleotide sequence capable of hybridising to SEQ ID NO: 3 under low

stringency conditions at 42°C.

9. An isolated nucleic acid molecule according to claim 7 comprising a nucleotide sequence substantially as set forth in SEQ ID NO: 4 or a nucleotide sequence having at least 40% similarity thereto or a nucleotide sequence capable of hybridising to SEQ ID NO: 4 under low stringency conditions at 42°C.

10. An isolated nucleic acid molecule according to claim 7 comprising a nucleotide sequence substantially as set forth in one or more of SEQ ID NOs: 5-29 or a nucleotide sequence having at least 40% similarity thereto or a nucleotide sequence capable of hybridising to one or more of SEQ ID NOs: 5-29 under low stringency conditions at 42°C.

11. An isolated nucleic acid molecule according to claim 1 wherein the length of the nucleic acid molecule is from about 50 bp to about 1500 kbp.

12. An isolated nucleic acid molecule according to claim 11 wherein the length of the nucleic acid molecule is from about 1 kbp to about 1000 kbp.

13. An isolated nucleic acid molecule according to claim 12 wherein the length of the nucleic acid molecule is from about 10 kbp to about 500 kbp.

14. An isolated nucleic acid molecule according to claim 13 wherein the length of the nucleic acid molecule is from about 10 kbp to about 100 kbp.

15. An isolated nucleic acid molecule comprising a nucleotide sequence encompassing a neocentromere or a functional derivative, synthetic or hybrid form thereof which when said nucleic acid molecule is in linear form and co-introduced into a cell together with a telomeric sequence, is capable of replicating, remaining as an extra-chromosomal element and segregates with cell division.

16. An isolated nucleic acid molecule according to claim 15 wherein the nucleotide sequence is derived from a mammalian chromosome.

17. An isolated nucleic acid molecule according to claim 16 wherein said nucleic acid molecule is capable of associating with CENP-A and CENP-C antibodies.

18. An isolated nucleic acid molecule according to claim 16 or 17 wherein the mammalian chromosome is human chromosome 10 or a modified form of chromosome 10 or its non-human mammalian or non-mammalian equivalent.

19. An isolated nucleic acid molecule according to claim 18 wherein the nucleotide sequence corresponds to a region mapping between q24 and q26 on chromosome 10.

20. An isolated nucleic acid molecule according to claim 18 wherein the modified form of human chromosome 10 is mardel (10) chromosome.

21. An isolated nucleic acid molecule according to claim 18 comprising a nucleotide sequence substantially as set forth in SEQ ID NO: 3 or a nucleotide sequence having at least 40% similarity thereto or a nucleotide sequence capable of hybridising to SEQ ID NO: 3 under low stringency conditions at 42°C.

22. An isolated nucleic acid molecule according to claim 19 comprising a nucleotide sequence substantially as set forth in SEQ ID NO: 4 or a nucleotide sequence having at least 40% similarity thereto or a nucleotide sequence capable of hybridising to SEQ ID NO: 4 under low stringency conditions at 42°C.

23. An isolated nucleic acid molecule according to claim 19 comprising a nucleotide sequence substantially as set forth in one or more of SEQ ID Nos: 5-29 or a nucleotide sequence having at least 40% similarity thereto or a nucleotide sequence capable of hybridising to one or more of SEQ ID Nos: 5-29 under low stringency conditions at 42°C.

24. An isolated nucleic acid molecule according to claim 15 wherein the length of the nucleic acid molecule is from about 50 bp to about 1500 kbp.

25. An isolated nucleic acid molecule according to claim 24 wherein the length of the nucleic acid molecule is from about 1 kbp to about 1000 kbp.

26. An isolated nucleic acid molecule according to claim 25 wherein the length of the nucleic acid molecule is from about 10 kbp to about 500 kbp.

27. An isolated nucleic acid molecule according to claim 26 wherein the length of the nucleic acid molecule is from about 10 kbp to about 100 kbp.

28. An isolated nucleic acid molecule or its chemical equivalent encompassing a human neocentromere or a functional derivative thereof or a latent, synthetic, hybrid or its mammalian or non-mammalian homologue.

29. An isolated nucleic acid molecule according to claim 28 wherein said nucleic acid molecule when introduced into a compatible cell is a replicating, extra-chromosomal element which segregates with cell division.

30. An isolated nucleic acid molecule according to claim 29 wherein the nucleic acid molecule is capable of associating with centromeric binding proteins (CENP)-A and -C or antibodies thereto.

31. An isolated nucleic acid molecule according to claim 29 or 30 wherein the chromosome is human chromosome 10 or a modified form of human chromosome 10 or its non-human mammalian or non-mammalian equivalent.

32. An isolated nucleic acid molecule according to claim 31 wherein the nucleotide sequence corresponds to a region mapping between q24 and q26 on chromosome 10.

33. An isolated nucleic acid molecule according to claim 31 wherein a modified form of human chromosome 10 is a mardel (10) chromosome.

34. An isolated nucleic acid molecule according to claim 31 comprising a nucleotide sequence substantially as set forth in SEQ ID NO: 3 or a nucleotide sequence having at least 40% similarity thereto or a nucleotide sequence capable of hybridising to SEQ ID NO: 3 under low stringency conditions at 42°C.

35. An isolated nucleic acid molecule according to claim 32 comprising a nucleotide sequence substantially as set forth in SEQ ID NO: 4 or a nucleotide sequence having at least 40% similarity thereto or a nucleotide sequence capable of hybridising to SEQ ID NO: 4 under low stringency conditions at 42°C.

36. An isolated nucleic acid molecule according to claim 32 comprising a nucleotide sequence substantially as set forth in one or more of SEQ ID Nos: 5-29 or a nucleotide sequence having at least 40% similarity thereto or a nucleotide sequence capable of hybridising to one or more of SEQ ID Nos: 5-29 under low stringency conditions at 42°C.

37. An isolated nucleic acid molecule according to claim 28 wherein the length of the nucleic acid molecule is from about 50 bp to about 1500 kbp.

38. An isolated nucleic acid molecule according to claim 37 wherein the length of the nucleic acid molecule is from about 1 kbp to about 1000 kbp.

39. An isolated nucleic acid molecule according to claim 38 wherein the length of the nucleic acid molecule is from about 10 kbp to about 500 kbp.

40. A genetic construct comprising an origin of replication for a eukaryotic cell and a nucleic acid molecule encompassing a eukaryotic neocentromere or a functional derivative thereof or a latent, synthetic, hybrid form thereof or its mammalian or non-mammalian homologue flanked by telomeric nucleotide sequences functional in the cell in which the genetic construct is to

replicate and wherein said genetic construct when introduced into a cell is a replicating, extra-chromosomal element which segregates with cell division.

41. A genetic construct according to claim 40 wherein the eukaryotic neocentromere is a mammalian centromere.

42. An isolated nucleic acid molecule according to claim 41 wherein the neocentromere is a human neocentromere.

43. An isolated nucleic acid molecule according to claim 42 wherein the nucleic acid molecule is capable of associating with CENP-A and -C or antibodies thereto.

44. An isolated nucleic acid molecule according to claim 43 wherein the neocentromere is from human chromosome 10 or a modified form of human chromosome 10 or its non-human mammalian or non-mammalian equivalent.

45. An isolated nucleic acid molecule according to claim 44 wherein the human neocentromere maps to a region between q24 and q26 on chromosome 10.

46. An isolated nucleic acid molecule according to claim 44 wherein a modified form of human chromosome 10 is a mardel (10) chromosome.

47. An isolated nucleic acid molecule according to claim 45 comprising a nucleotide sequence substantially as set forth in SEQ ID NO: 3 or a nucleotide sequence having at least 40% similarity thereto or a nucleotide sequence capable of hybridising to SEQ ID NO: 3 under low stringency conditions at 42°C.

48. An isolated nucleic acid molecule according to claim 46 comprising a nucleotide sequence substantially as set forth in SEQ ID NO: 4 or a nucleotide sequence having at least 40% similarity thereto or a nucleotide sequence capable of hybridising to SEQ ID NO: 4 under low stringency conditions at 42°C.

49. An isolated nucleic acid molecule according to claim 46 comprising a nucleotide sequence substantially as set forth in one or more of SEQ ID Nos: 5-29 or a nucleotide sequence having at least 40% similarity thereto or a nucleotide sequence capable of hybridising to one or more of SEQ ID Nos: 5-29 under low stringency conditions at 42°C.

50. An artificial chromosome for use in gene therapy said artificial chromosome comprising a nucleic acid molecule capable of conferring a phenotypic property on a cell carrying said artificial chromosome wherein said artificial chromosome is a replicating element which segregates with cell division.

51. An artificial chromosome according to claim 50 wherein said artificial chromosome is capable of functioning in a mammalian cell.

52. An artificial chromosome according to claim 51 wherein said artificial chromosome is capable of functioning in a human cell.

53. An artificial chromosome according to claim 52 wherein the chromosome is a human chromosome.

54. An artificial chromosome according to claim 53 wherein the chromosome is capable of associating with CENP-A and -C or antibodies thereto.

55. An artificial chromosome according to claim 53 or 54 wherein the chromosome is human chromosome 10 or a modified form of human chromosome 10 or its non-human mammalian or non-mammalian equivalent.

56. An artificial chromosome according to claim 55 comprising a region mapping between q24 and q26 on chromosome 10.

57. An artificial chromosome according to claim 5 wherein a modified form of human chromosome 10 is a mardel (10) chromosome.

58. An artificial chromosome according to claim 56 comprising a nucleotide sequence substantially as set forth in SEQ ID NO: 3 or a nucleotide sequence having at least 40% similarity thereto or a nucleotide sequence capable of hybridising to SEQ ID NO: 3 under low stringency conditions at 42°C.

59. An artificial chromosome according to claim 57 comprising a nucleotide sequence substantially as set forth in SEQ ID NO: 4 or a nucleotide sequence having at least 40% similarity thereto or a nucleotide sequence capable of hybridising to SEQ ID NO: 4 under low stringency conditions at 42°C.

60. An artificial chromosome according to claim 57 comprising a nucleotide sequence substantially as set forth in one or more of SEQ ID Nos: 5-29 or a nucleotide sequence having at least 40% similarity thereto or a nucleotide sequence capable of hybridising to one or more of SEQ ID Nos: 5-29 under low stringency conditions at 42°C.

61. An isolated nucleic acid molecule comprising a sequence of nucleotides which defines a eukaryotic neocentromere.

62. An isolated nucleic acid molecule according to claim 61 wherein the neocentromere is derived from a mammalian chromosome.

63. An isolated nucleic acid molecule according to claim 61 wherein the neocentromere is derived from a human chromosome.

64. An isolated nucleic acid molecule according to claim 63 wherein the nucleic acid molecule is capable of associating with centromeric binding proteins (CENP)-A and -C or antibodies thereto.

65. An isolated acid molecule according to claim 63 or 64 wherein the chromosome is human chromosome 10 or a modified form of human chromosome 10 or its non-human mammalian or non-mammalian equivalent.

66. An isolated nucleic acid molecule according to claim 65 wherein the nucleotide sequence corresponds to a region mapping between q24 and q26 on chromosome 10.

67. An isolated nucleic acid molecule according to claim 65 wherein a modified form of human chromosome 10 is a mardel (10) chromosome.

68. An isolated nucleic acid molecule according to claim 66 comprising a nucleotide sequence substantially as set forth in SEQ ID NO: 3 or a nucleotide sequence having at least 40% similarity thereto or a nucleotide sequence capable of hybridising to SEQ ID NO: 3 under low stringency conditions at 42°C.

69. An isolated nucleic acid molecule according to claim 67 comprising a nucleotide sequence substantially as set forth in SEQ ID NO: 4 or a nucleotide sequence having at least 40% similarity thereto or a nucleotide sequence capable of hybridising to SEQ ID NO: 4 under low stringency conditions at 42°C.

70. An isolated nucleic acid molecule according to claim 67 comprising a nucleotide sequence substantially as set forth in one or more of SEQ ID NOs: 5-29 or a nucleotide sequence having at least 40% similarity thereto or a nucleotide sequence capable of hybridising to one or more of SEQ ID NOs: 5-29 under low stringency conditions at 42°C.

71. An isolated nucleic acid molecule according to claim 61 wherein the length of the nucleic acid molecule is from about 50 bp to about 1500 kbp.

72. An isolated nucleic acid molecule according to claim 71 wherein the length of the nucleic acid molecule is from about 1 kbp to about 1000 kbp.

73. An isolated nucleic acid molecule according to claim 72 wherein the length of the nucleic acid molecule is from about 10 kbp to about 500 kbp.

74. An isolated nucleic acid molecule according to claim 73 wherein the length of the nucleic acid molecule is from about 10 kbp to about 100 kbp.

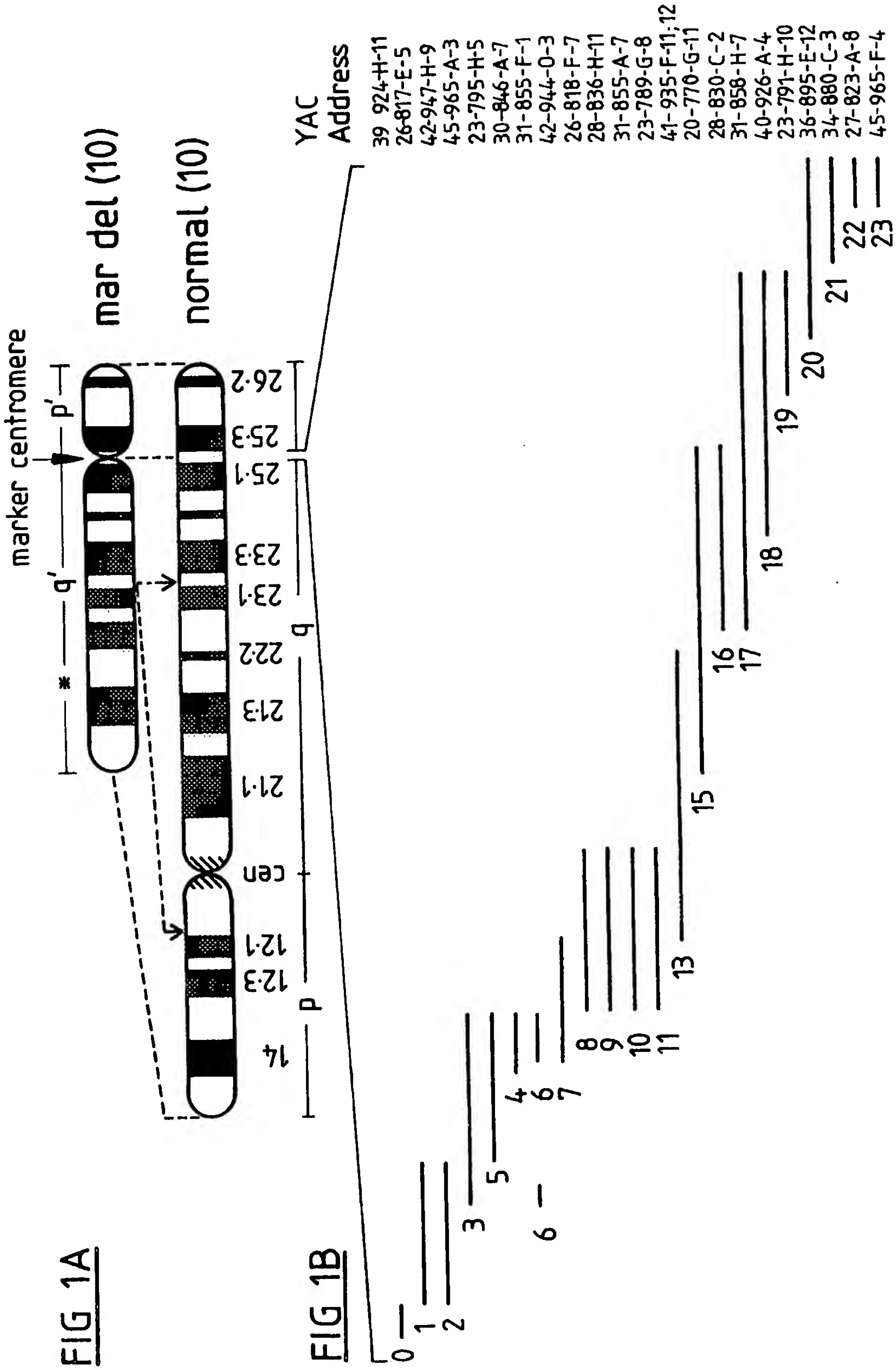
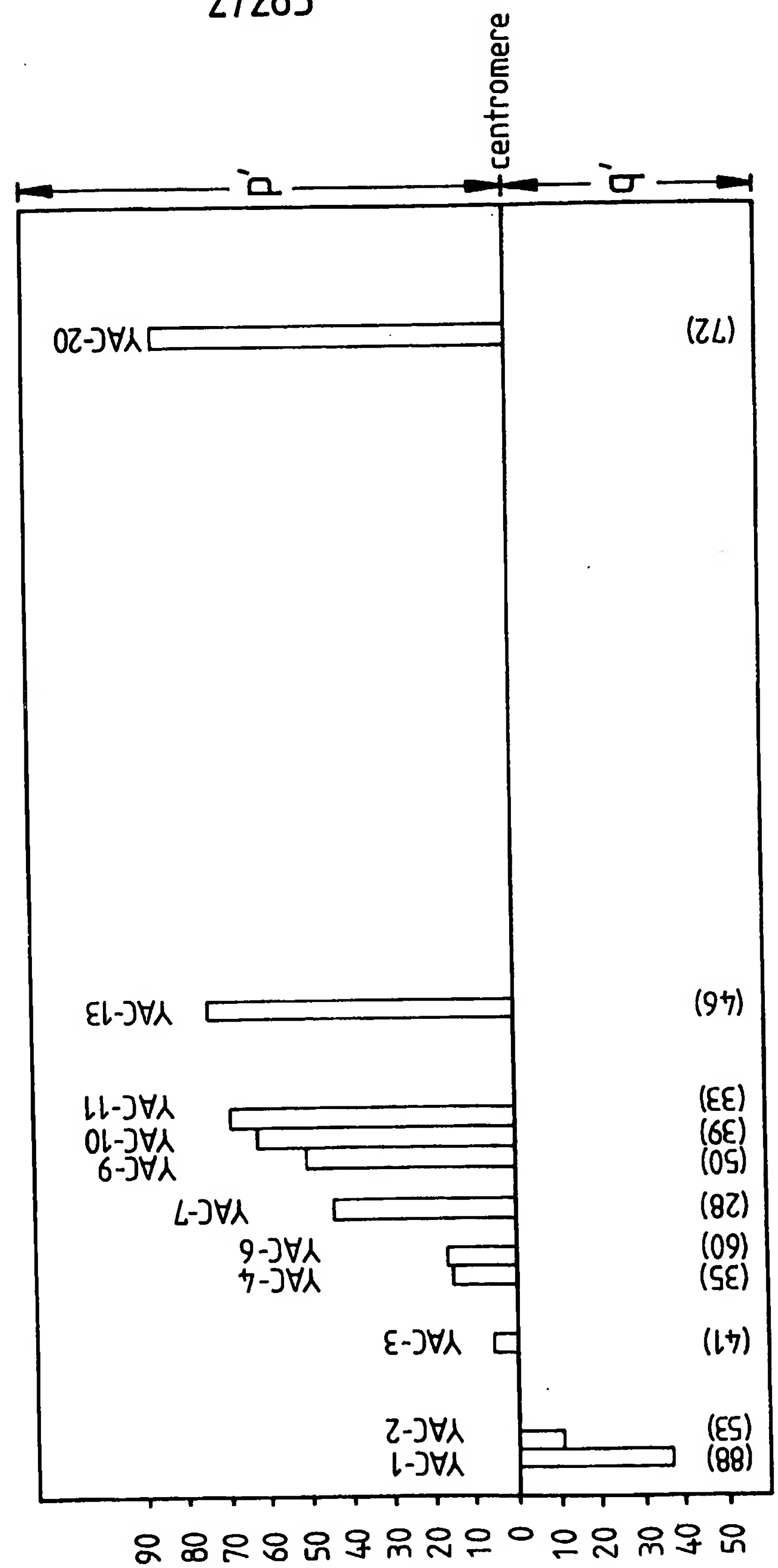

marker centromere
mar del (10)
normal (10)
p'
q'
*
26·2
25·3
25·1
23·3
23·1
22·2
21·3
21·1
cen
12·1
12·3
14
p
q
YAC
Address
39 924-H-11
26-817-E-5
42-947-H-9
45-965-A-3
23-795-H-5
30-846-A-7
31-855-F-1
42-944-0-3
26-818-F-7
28-836-H-11
31-855-A-7
23-789-G-8
41-935-F-11,12
20-770-G-11
28-830-C-2
31-858-H-7
40-926-A-4
23-791-H-10
36-895-E-12
34-880-C-3
27-823-A-8
45-965-F-4

FIG 1A

FIG 1B



centromere
p'
q'
YAC-20 (72)
YAC-13 (46)
YAC-11 (33)
YAC-10 (39)
YAC-9 (50)
YAC-7 (28)
YAC-6 (60)
YAC-4 (35)
YAC-3 (41)
YAC-2 (53)
YAC-1 (88)
90 80 70 60 50 40 30 20 10 0 10 20 30 40 50

FIG 1C

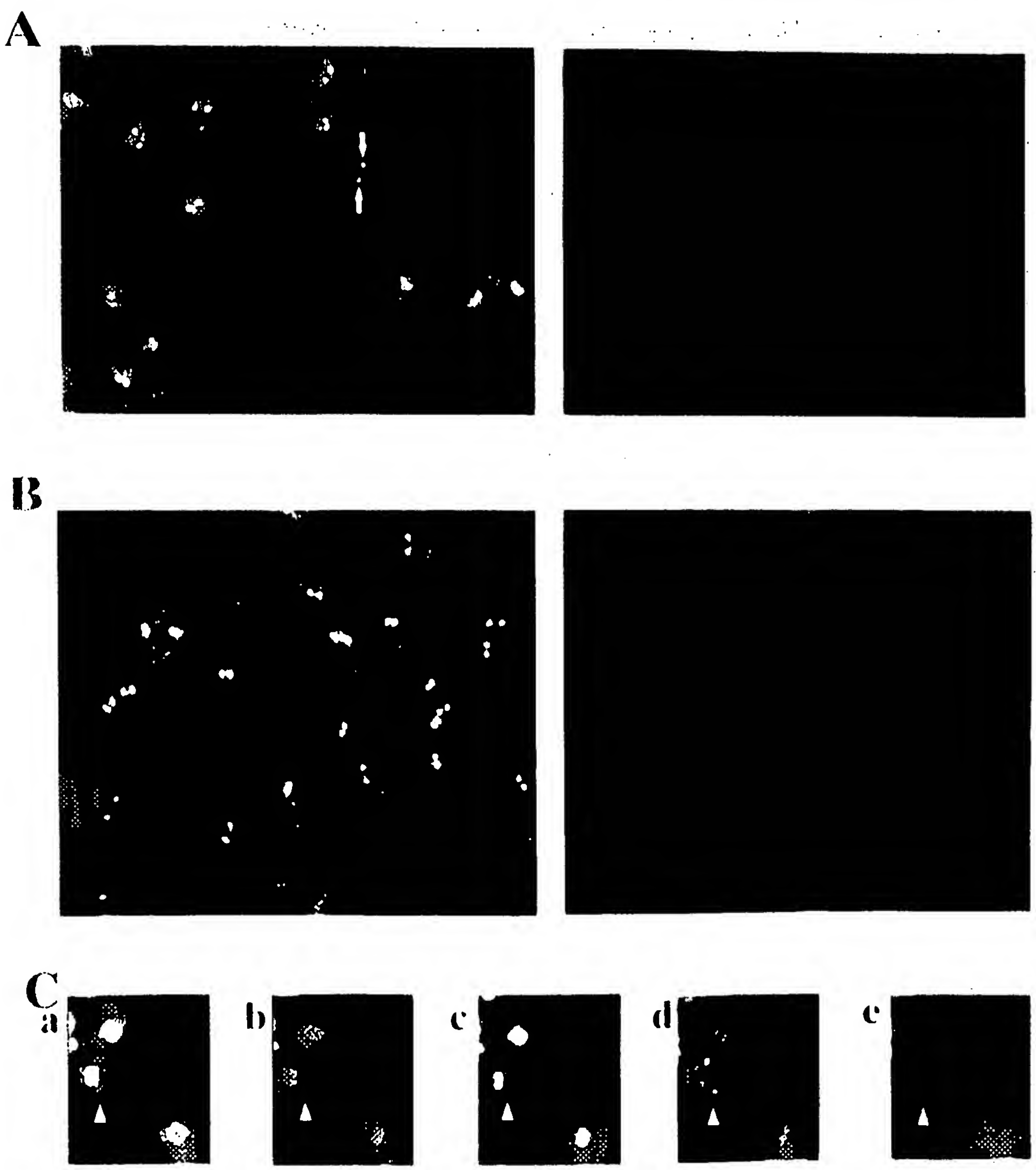


FIG 2

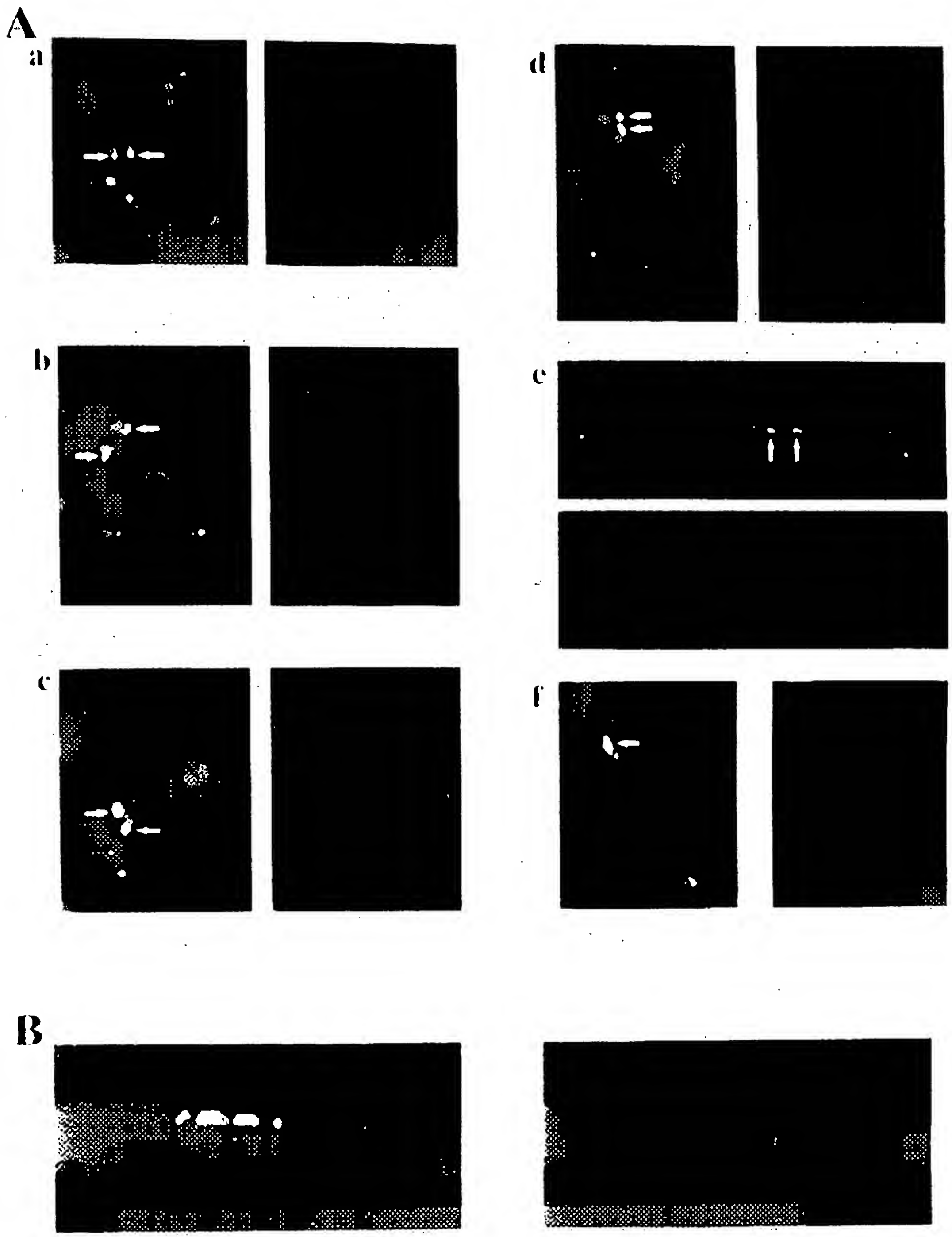


FIG 3

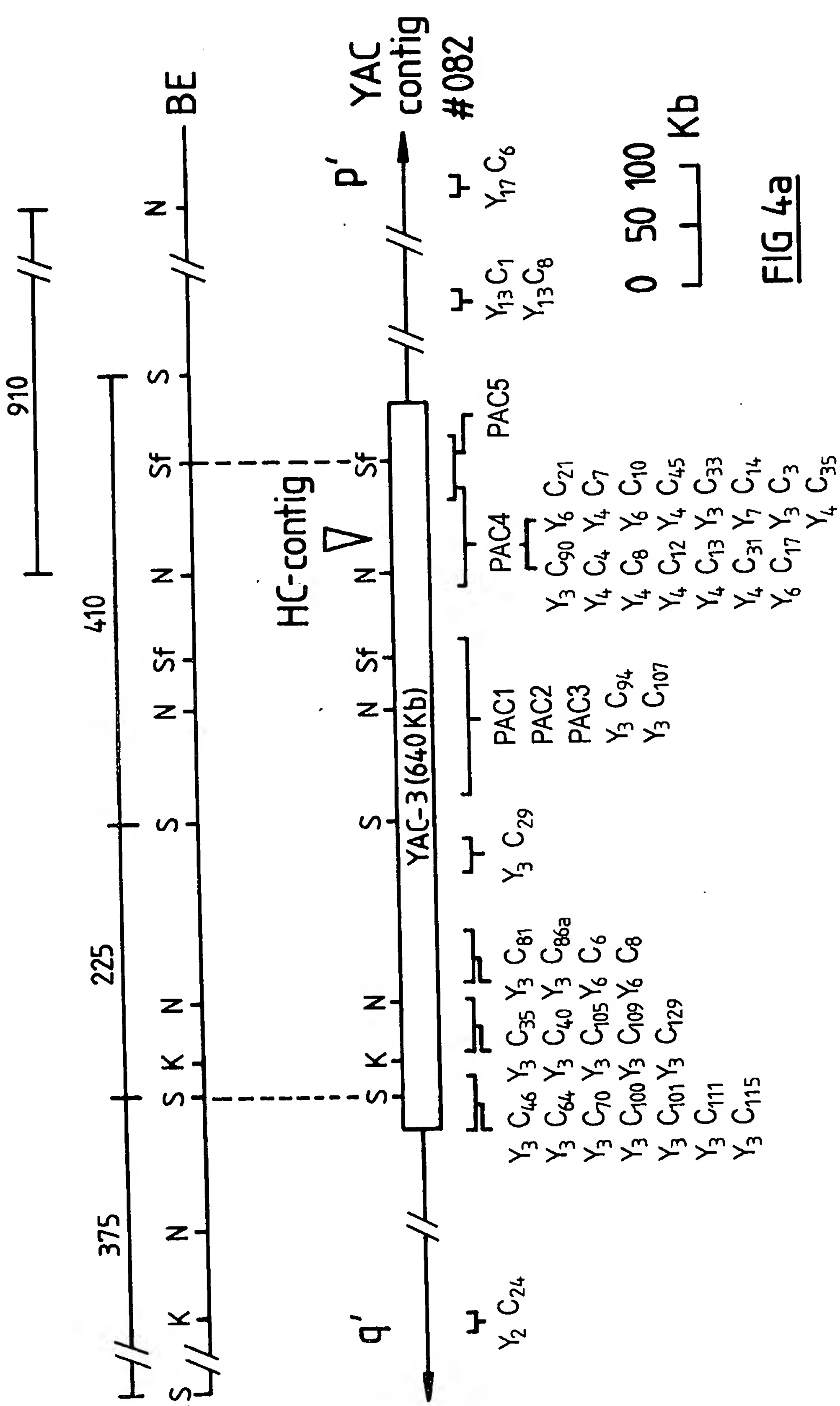

910
410
225
375
BE
YAC contig #082
p'
q'
HC-contig
YAC-3 (640Kb)
PAC1
PAC2
PAC3
PAC4
PAC5
0 50 100 Kb

FIG 4a

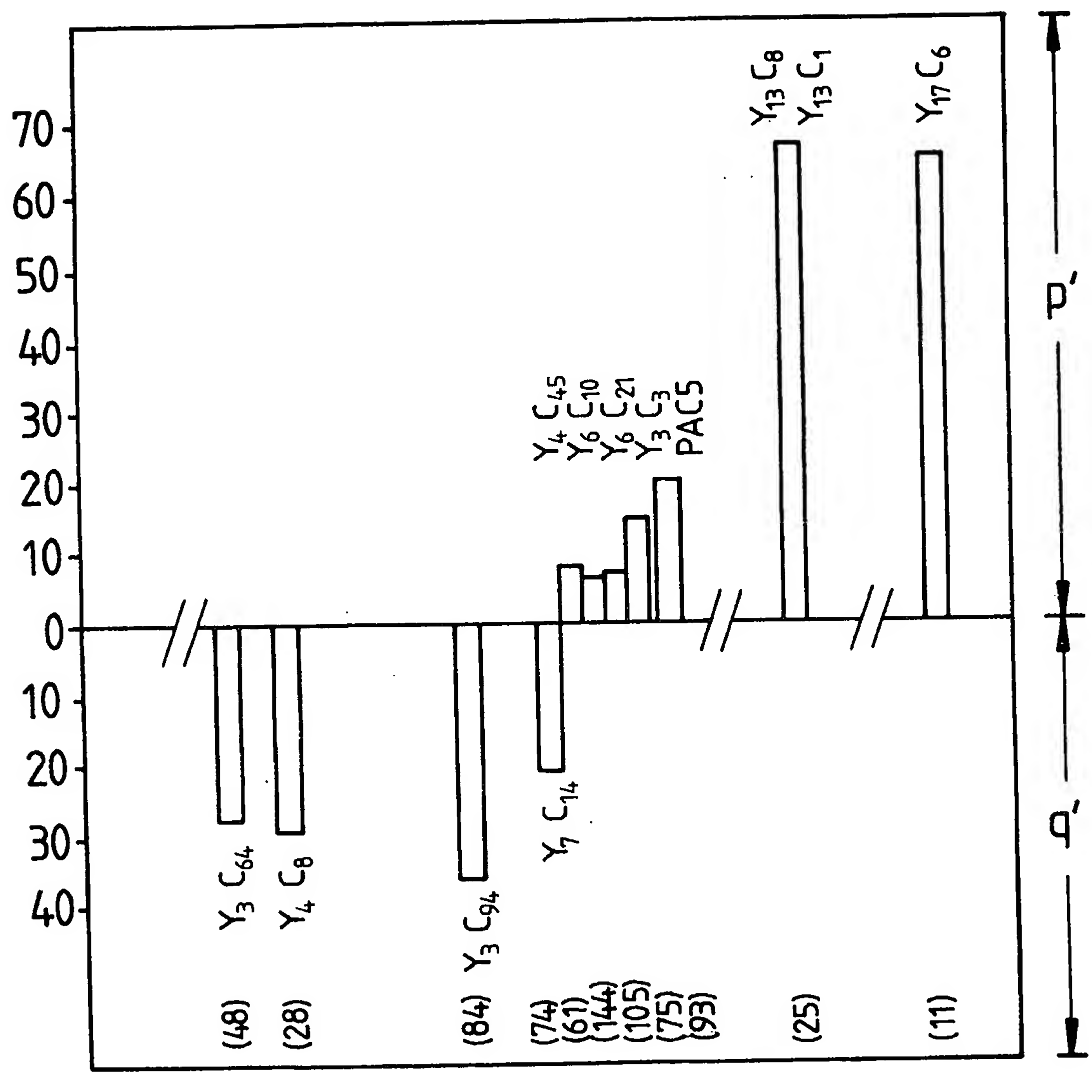

70
60
50
40
30
20
10
0
10
20
30
40
Y3 C64
Y4 C8
Y3 C94
Y7 C14
Y4 C45
Y6 C10
Y6 C21
Y3 C3
PAC5
Y13 C8
Y13 C1
Y17 C6
(48)
(28)
(84)
(74)
(61)
(144)
(105)
(75)
(93)
(25)
(11)
p'
q'

FIG 4b

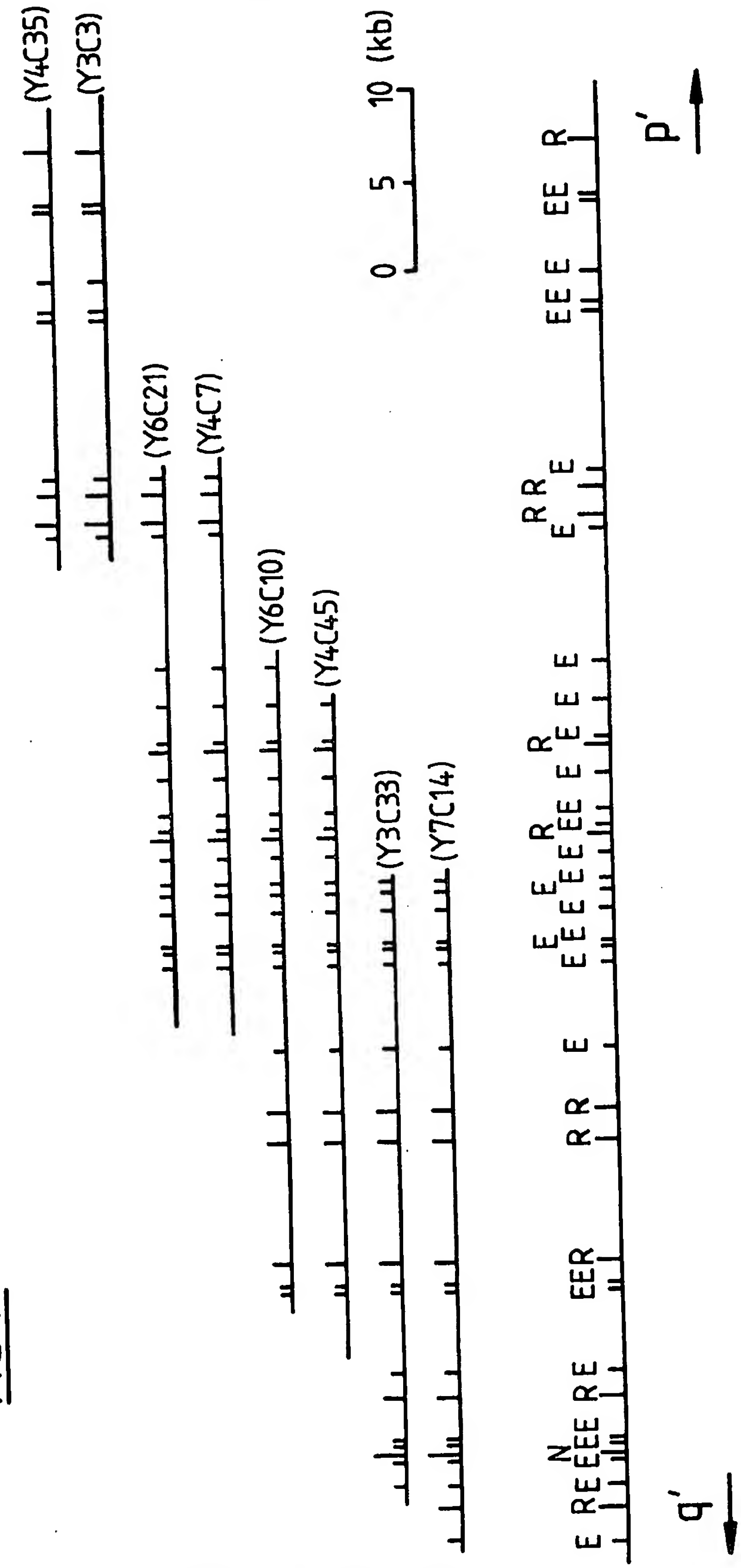


FIG 4c

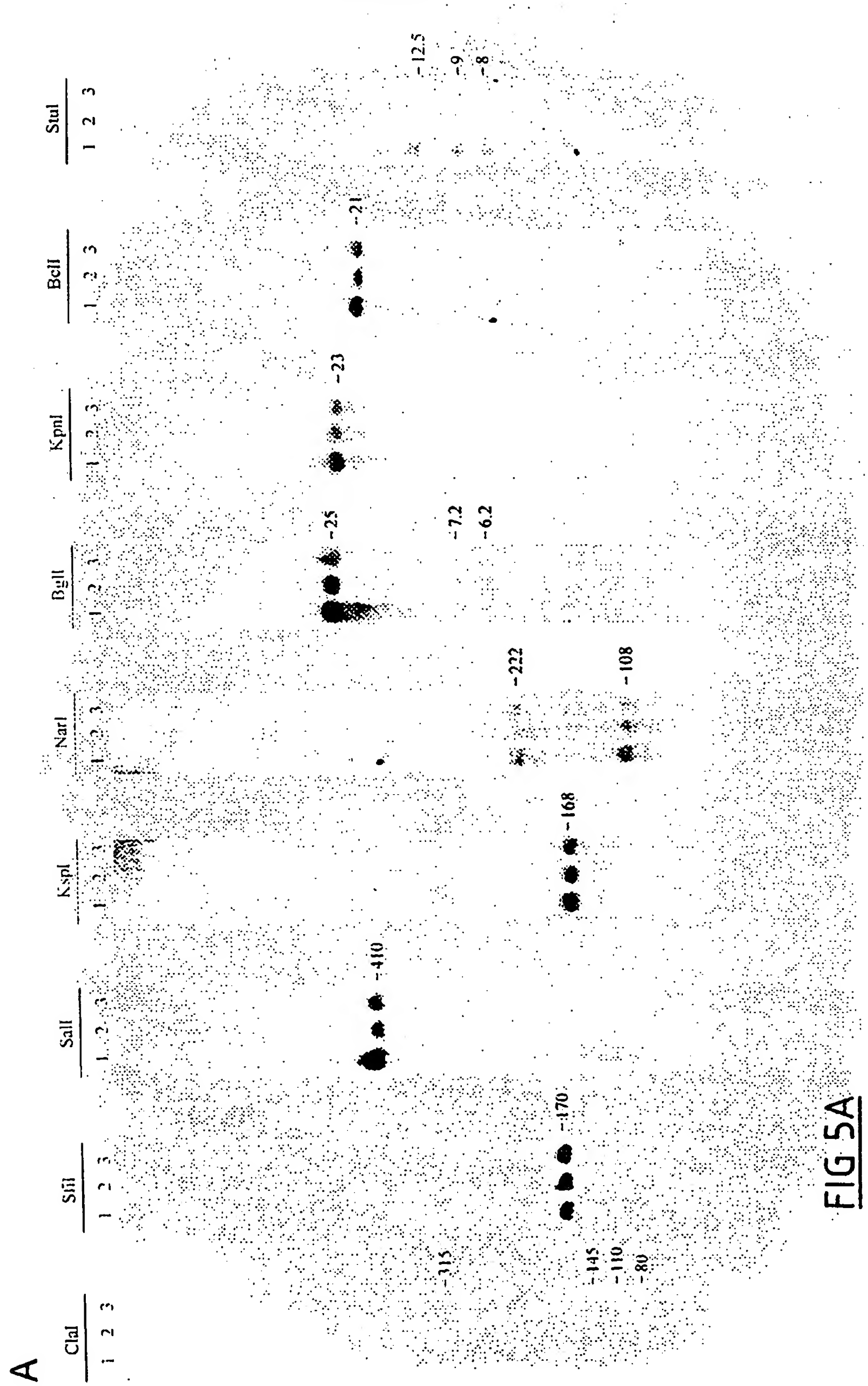

A
ClaI
SfiI
SalI
KspI
NarI
BglI
KpnI
BclI
StuI
-315
-145
-110
-80
-170
-410
-168
-222
-108
-7.2
-6.2
-25
-23
-21
-12.5
-9
-8

FIG 5A

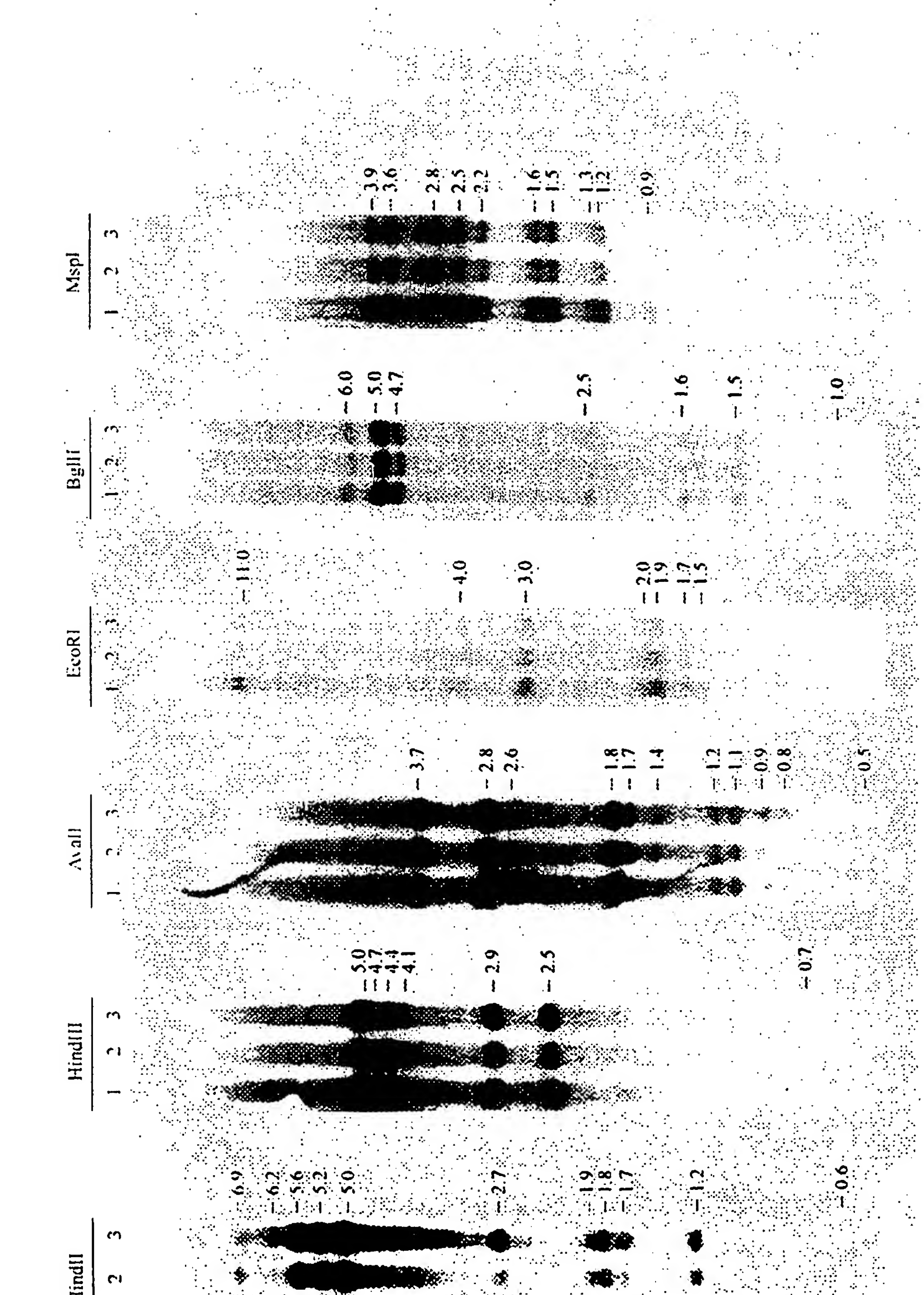

B
HindII
1 2 3
6.9
6.2
5.6
5.2
5.0
2.7
1.9
1.8
1.7
1.2
0.6
HindIII
1 2 3
5.0
4.7
4.4
4.1
2.9
2.5
0.7
AvaII
1 2 3
3.7
2.8
2.6
1.8
1.7
1.4
1.2
1.1
0.9
0.8
0.5
EcoRI
1 2 3
11.0
4.0
3.0
2.0
1.9
1.7
1.5
BglII
1 2 3
6.0
5.0
4.7
2.5
1.6
1.5
1.0
MspI
1 2 3
3.9
3.6
2.8
2.5
2.2
1.6
1.5
1.3
1.2
0.9

FIG 5B

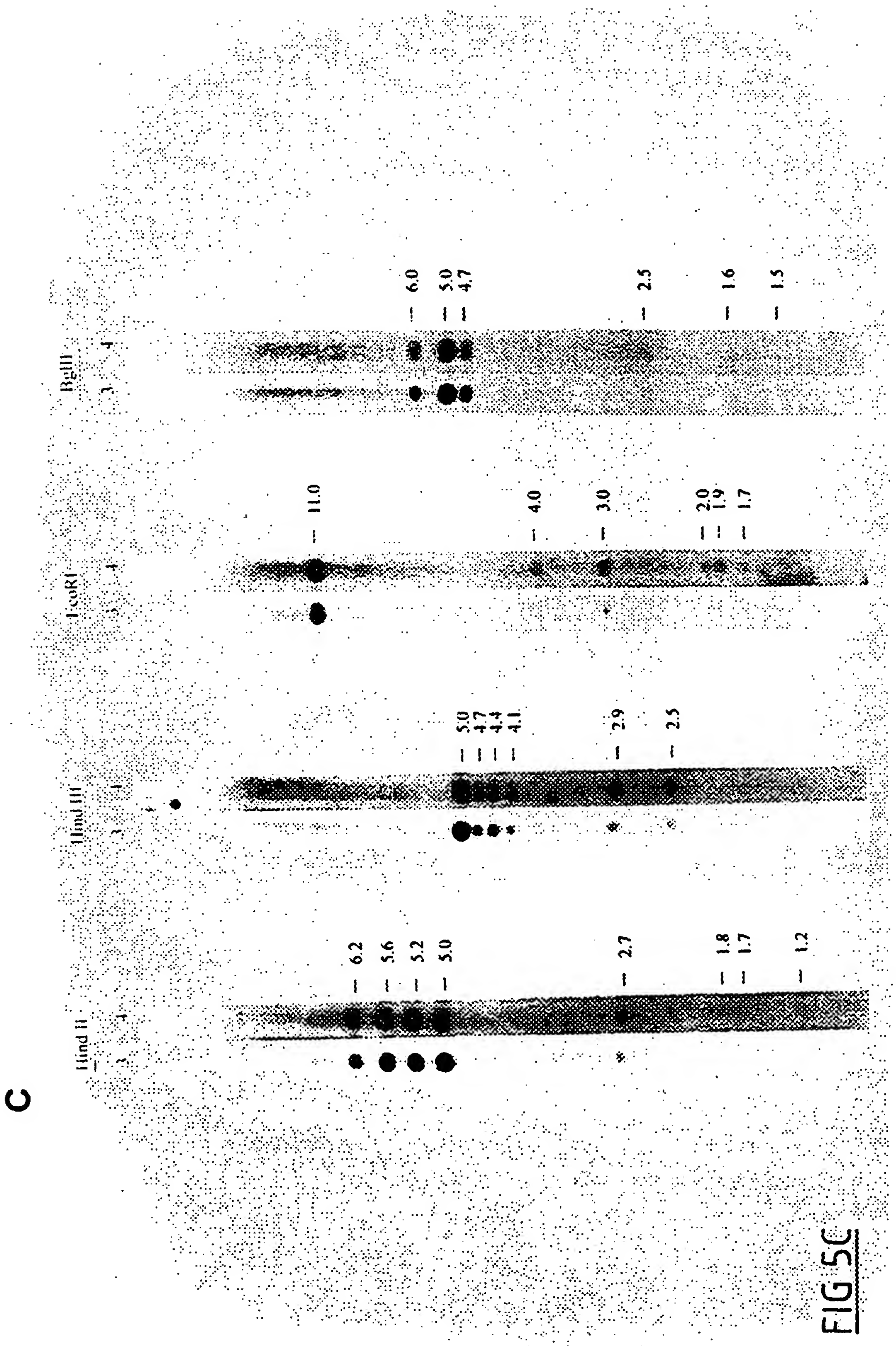

C
Hind II
3
4
6.2
5.6
5.2
5.0
2.7
1.8
1.7
1.2
Hind III
3
4
5.0
4.7
4.4
4.1
2.9
2.5
EcoRI
3
4
11.0
4.0
3.0
2.0
1.9
1.7
BglII
3
4
6.0
5.0
4.7
2.5
1.6
1.5

FIG 5C

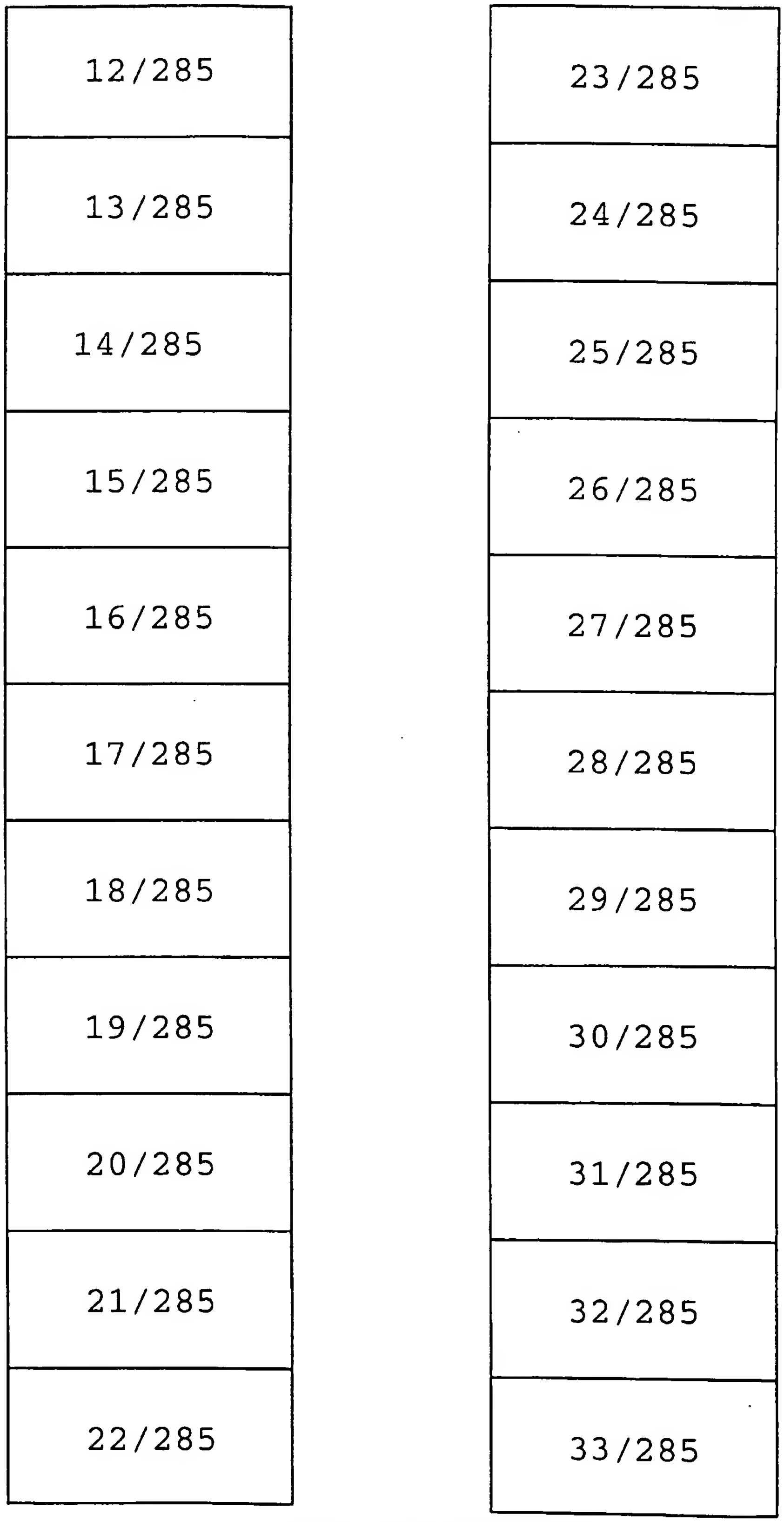

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FIGURE 6 (1)

GAATTCTCCT GCCTCAGCCT CCCAAGTAGC TGAGGTTACA GGTGCCAGCC ACCACGTCCA

GCTAATTTTT GTATTTTAGT AGAGACGGGG TTTCACCGTG TTTGCCAGGC TGGTATCAAA

CTCCTGACCT CAAGTGATCT GCCTGCCTCA GCCTCCCAAA ATGCTAGGAT TACAGGTGTG

AGTCACCGCA CCCAGCCCTT CTTTCAGTTC TATCACCTCT TTTTGCTATA TTTGTATGAG

AGCTTTATTA TTAGGGGCAC ATACATTTAA AATTGTTATG TCTTATTGAT AGATTGATCT

GTCATTATGA ATGTCTGTAT TCATTCCCTG ATAGTATTTC TTTTTCTAAA TATTTTTCTG

AATGTGTCTG CTATTAACAT AGCCACTCTG GCTTTTTAAA ATTAGTATTT TTATGGTATA

TATTTTTCCT TTTTTTTTTT TTTAAGTTTT AGATGTTATG TTTCCTTATA CTTAAAGTGG

GTGTCTTATA GGCAGCATAT ATCTGGGTCT TGATGTATTA TTTAATCTGA TAATCTCAAC

CTTTTTGTTG GAGTGTTTAG GCCATTTACA TTTAGTGTAA TTATAGACAT GGTTTGATTT

GCTATACCAT CTTTTCATTT GTTTTATATG TGAGCCATCT TTTCATTGTT CTTTTTTCAT

FIGURE 6 (2)

CTTTGACCAT TTTCTTTAGT ACTGAATACT TTTTTTGTAT TTCATTATAT CTATTGGCTT

TTTAGTTATA CCTCTTAAAA TTTTTTTTTC TGTTTTATGT AGGATTTATA ATATACATCT

TTAACTTATC ACAGATTACC TTCAAATAGT ATTTTACCAG CTCAAGTGTA ATGTAGAAAC

CTTACAAGAG TATATTTTCA TTTCTGTCTC CTAATTTTTA TGCTATGTCT ATAATACATT

AGGTTTGTTG TTGTTTGTTT TTACCTTATT GCTGTTGGCT GGGGTCAGCA AACATTTTCT

GTAAAGGGCT AGATAGTACA GGCATACCTT GGAGATACTG TGGGTTTGGT TCCATACCAC

CACAATAATA CAAATATGCA AGAAGTGGAT ATCACAATAA AGTGAGTCAC ACAAGTCTTT

TGGCTTCCCA GTGCATATAA AAGTTTTGCT TATACTACAC TGTAGTCTGT TAAGTGTGCA

ATAGTGTTAT GTCTAAAAAA ACACATACCT TAATTTTAAA ATGCTTTATT ACTAAAAAAT

GCTAACAATC ATTTGAGCAT TCAGTGAGTT GTAATCTTTT TGCTGGTGGA AGGTCTTTTC

TTATTGATGA CTGATCGGGG GTCAGGTGCT GAAGCTTAGG GTGGCTGTGG CAGTTTCTTA

FIGURE 6 (3)

AAACAACAGT GAAGATTGCA ATATCAGTTG ACTCTTCCTT TCATGAAAGA TTTCTCTCTA

GTGTGTGATG CTTTTTGATA GCATTTTATG CACAGTAGAA CTTCTTTGAA AATTGGATCA

ATCCTCTCAA ACCCTGCTCT GCTTTAACAA CCTAAGTTAA TATAATATTC TGAATCCATT

GTTGTCATTT CAACAATTTT CACAGTGTCT TCACCAGGAG TAGATTCCAT CTCATTTCCT

GAGATGGAAT CTTTGCTCAT CCATAAGAAG AAATTCCTCA TCTGTTCAAG TTTTATCATG

AGATTGCAGC AATACAGTCA TGTCTTCAGG CCTCACTTCA CTTTTAATTC CAGTTCTCTT

GCTGTTTCTA CCACATCTGT GGTTCCTTCC TCCATTGAAG TCTTGAACCT CTCCAAGTCA

TCCATGAGGG TTGGAATCGA CTTCTTCCAA ATTCCTGTTA ATATTTATAT TTTGACCTCC

CATGAATCAT GAATGTTCTT AATGGCACCT GGAATGGTGA ATCCTTTCCA AAAGGTTTTC

AATTTACTTA GTCCAGATCC ATCCATCCAG AGGATCCACT TTCAATGCCA GTTATAGCCT

TATGGAATGT ATTTCTTCAA TAATAAGGCT TGAAAGTTGA AATTACTCCT TGATCCATTT

FIGURE 6 (4)

TCTGCAAAAT AGATGTTGTG TTAGCAGGCA TGAAAGCAAC ATTAATCTTT TTGTACATGT

CCATCAGAGC TCTTGGGTGA CCAGGTATAT TGCCAGTGAG CAGTAATACT TTGAAAGGAA

TTATTTTTCT TAGCAGTAGG TCTCAACAAT GGGCTTAAAA TATTTGGTCC ACCATTCTGT

AAACTGATGT GCTGTCATCT AAACTTTGTA GTTTCATTTA TAGAGCACAG GCAGAGTAGA

TGTAGCATAA TTCTTAAGGG ACTTAGGATT TTCAGAATGG TAAATGAACA TTGGCATCAA

TTTAAATCAC TAGCTGTATT AGCCCCCAAC AAGAGAGTCA GCCTATTTTT TGAAGCTTTG

AAGCCAAGCG TCGACTTCTC CTCCCTGGTT ACAAAAGTCC TAAATGGCAT CTTCTTCCAA

TATAAGGCTG TTTTATCTAC ATTGAAAATC TGTTGTTTAG TGTAGCCACC TTCATCAATG

ATACTATCTA GATCTCTTGG ATAACTTGTG CAGCTTCTAC ATCAGCATTT GCTACTTCAC

CTTGTACTCT TATGTAATGG AGTGGCATCT TTCCTCGTAC CTCATGAACC AACCTCTGCT

AGCTTCCAAC TTTTCTTCTG TAGTTTCCTC GCCTCTCTCA GCCTTCATAG ACTTGAGGAT

FIGURE 6 (5)

AGTTAGAGAC TTGCTTTGGA TTAGATTTTG GCTTCAGGAA ATGTTGTGGC TGGTTTGATC

TTCTATCCAG ACCACTAAAA CTTTATCCAT ATCAGCAATA AGGCTGTTTT GCTTTCTTAT

TATTTGTGTG TTCACTGGAG TAGCACTTTT AATTTGCTTC AAGATATATT TCTTTGCATT

CACAACTTGG CTGACTGGTG CAAGAGGCCT AGCTTTCAGA CTATCTTGGC TTTTGACATG

CCTTCCTCAC TAAGCTTAAT CATTTCTAGC TTTTGATTTA AAATGAGAGA TGTAGGCCAG

GCACAGTGGC AGGCACAGTG GCATATGCCT GTAATTCCAA CACATTAAGA GGCCAAGGTG

GGAGGATTGC TTGAACCCAG GAGGTGGAGG TTGTAGAGAT CACACCACTG CATTCCGTCC

TGGATGACAG AGCAAGACCT TTCTCAAAAT AAAATGAGAG GTGTGCTTCT TCTTTTTGTT

TGAGCCCATA GAAGCCATAG TATGATTTTT AATTGGCCTA ATTTCAATAC TGTTGTGTCT

CAGAGAATAG GGAGGTCTGA AGAGAGGGAG AGAGGTGGGG GAATGGCTGG TCAGTGGAGC

AGTCAGAACA CACATAACAC TAATAAATTG TTTGCTGTCT TATATGGATG TGGTTTGTGA

FIGURE 6 (6)

TGCCCCCAAA CAATTACAAT AGTTACAGCA AATATCACTG ATCACAGATC ACCATAACAG

ATATAAGAAT CATGGCAAAG TTTGAAATAT TCTTGAGAAT TAGCAAAGTG TGACACAGAG

AAACAAAGTG AGCACATGCC GTTGGAAAAA ATTGGTGTTG ATAGACTTGC TCCATCGCAA

GTTTGCCATA CGCCTTCAAT TTATAAAAAA CACAATATCT AGGAAGTTCA ATAAAGTGAA

GTGCAATAAG ATGAAGTATG CCTGTAAATA TTTCAGGCTT TCCAGACCAT AGGGTTTCTG

TTGCAACTGC TCACCTCTGC CATTATAGCA TGAAAGCAGC TATAGAAAAT ATACATAAAT

GAGGCCTGTA ATCCCAACAC TTTGGGAGCC CAAGGTGGAT GGATCACTTG AGGTCAGGAA

TTCGAGACCA GCTTGGCCAA CATGGCAAAA CCCCGTCTCT ACTAAAAATA CAAAAATGAG

CCAGGACTAC GCATGCCTGT AGTCCCAGCT ACTTGGGAGG CTGAGGCAGG AGAATCTCTT

GAACCCGGGA AGGGGAGGTT ACAGTGAGCC AAGATTGTGC CACTGCACTC CAGCCTGGGC

AACAGAGTGA GACTGTCTCA CAAAAAAAAA AAAAGGAAAA GAAAATACAC ATAAATGAAT

FIGURE 6 (7)

GTATGTGGCT GTGTACCAGT ATATCCTCAT GCTCTAGCTT GCCAACCCTT GCTTTACACT

GTCAGTTACC TTCTAAAGAG ATTAAAAATC ATAACAATAT CTATTACGTT TATTCACATC

CTAGTGTCAT TTCTTCCTTA TGTAGAATCA AATTTCATTC TGGTATCATA TTTCTTCTTT

CTAAATAATT TCCTTTAATA TTTTTTATAG CACAGGTCTA ATAGCAATGC ATTATGCAAT

TCATTGCTAT TAGACCTGTG CTATAAAATA GCAATGAATT ATGTCAGTTT TTATTTGTCT

GAAAAAGTTT TTTGTTTTTG AAATATACTT TTGCTGGGTA TATAAATCCA TGTTGCATAA

CTTCTCTTTT CTTCAGCACT TTAATGAAGT CACTCAGTTA TCTTCTGGCT TGTATAGTTT

CTCTGGCTGC CTTCAAGATT TTTTCATTGT CTTTAATTTT TAGCAGTTTG ATGTGTCTAG

GAGTGATTTT CTTTGTATTT ATCCTTTTGG GGGCCTCTTA ATTTCTTTGA TCCTTTTTTT

CTTTTTTTTT TTTTTTTAAT CAGTTTTGGT CTGTCTCCTC AAGTGGGCTG AAAAAAAAAG

AAAAATAAAA TCATAGTTTA AAAAACTAAT TTTGGAAAAT TTTCAGCTAT CATTTCTTCA

FIGURE 6 (8)

AATATTTATC CTACTCTATG CTCCCCTCCT CCCCTTTCCT TCTGTGACTC AAATTACAGG

TATATTTAAC CATTTTATTT GTTCACGGCA CTTGGATGCT CTGCTTTCTT ATTTTTTGTC

TTTCATTTTG GATAATTTCT ACTGACCTAT CTTCAAGTTC ACTGATTCTT TTCTCAGTCA

TATCTAGTGT GCTCAACGCC TGTTGAAGAA ATCCTTTGTC TTTAATATCA TGTTTTTTAT

TTCTAGCATT TTCATGTAAC TCTTTGTTCT GGTTTCCATC TCTCTACTCA CTTTTTTTTT

TTTTTTTTTT TTTTTTTGAG ACAGAGTCTC GCTCTGTCAC CCAGGCTGGA GTGTAGTGGC

GCGATCTCGG CTCACTGCAA CTTCCGTCCC CTGGGTTCAA GTGATTCTCC TGCCTCATCC

TCCCGAGTAG TTGGAATTAC AGGTGCCCAC CACCGTGGCT GGCTAATTTT TGTATTTTTT

TAGTGGAAAC AGGGTTTCAC CATGTTGGCC AGGCTGGTCT TGAATTCCTG ACCTCAGGTG

ATCCACCTGC CTCAGCCTCC CCAATTGCTG AAATTACTGG CATGAGGCAC TGCACCCAGC

TCTGCTGACA TTTTTATCT TTTGCTGCAT TTTGTCTACC TTTTCCATGA AATCCTTTAA

FIGURE 6 (9)

CATAGTAGTC ATAGTTACTT TCAATTCCTT GTCTGACAGT TCTGACATTC AAGTCTAGGT

CTGTTAATAG CTTTGTGAGT CTGTTAACAG CTTTTTTTCA TTCTTGTCTG TGTGTTTTGT

ATTTCTTGAT TGTATGCCAA ATATTGCCTG TAAAATAAAC TTAGATAAGT CATACTTCTA

TCCAGAAATA GGCACATTTT TTGTGTCCAG TCATTAGTGT GGAGGGAGGT TGGGGCAGTC

TAGTCAGTGG CTGAACTAGG TTTGGATTTG TTGATGCTAT ACTTAGAATG CACCAGACTT

CCATTCACTG CAAGAGTGGG CTGCTGCGCT TTGTGATTCA TGTGAGGCCT GAATTGTGGG

TTTTTCCTTA GTGTGTCCCT CCATGCTCAG ATTTCAGCAA GTCTTCATAT CTGTGCCACA

GAAGGAATCT GACCCATGCT CTTTTTGACC TCCCCAAGTG ATCAACTGTT GCTTGTTATA

GCTTGTCATG GAGTAAGAGG GTGTTTTTTT AGTTTTCATC CTCCAGCCTT GGTCTTGGGC

CCTGAGCTCC TAGACTCCAG GAGTGGATGG AATCCAGTGA TTTCTCAGTA ATTCAGCCCC

TTCTCCAGTA GTGGCAGATC TCTGCTTTGT ATCAGTGCAA GATCCTGGGC TGAGCTCATT

FIGURE 6 (10)

TTCTGCCCTT CCTCGAGTGG CAGACAGCTC TTGCTTTCAC CCTTCTACCA AAGGCAGTGC

ATCTTTTCTT GGGCCTCTCC CCATTGAACT TATGACTTTC ACATAAGAGA AGGGCTCATG

TATCAGAGAA TTCTGTGACT TTGTGCCACA TACAGAGTCT CTCAGTTCTC TTGCCCTGCC

CCAGTCTTTT TTGTGAGCAC CTAGTAGAGA CCCTTGGAGA AGAGCAAGGA AGCGAGTATG

GACTTCTTTT GTGTCTGTCG ATTGCTTTGT TTCTCAACTG CTACTCTTGG ACTTTAAGAA

TTCATTAAAA TTTCAGCTGT TTTCTTTTAT TCTTTTTGTT TTTCTTTTTT TTTTTTTTTT

TTTTTAGATG GAGTCTTGCT CTGTTGCCCA GGCTGGAGTG CAGTGGTGTG ATCTTGGCTT

GCTGCAACCT CCGCCTCCCG GGTTCAAGCG ATTCTCCTGC CTCAGCCTCC CAAGTAGTTG

GGATTACAGG TGCCCACCAC CACACCTGGC TAATTTTTGT ATTTTTAGTA GACACAGGGT

TTCACCATTT TGGTCAGGCT TGTCTCAAAC TCCTGACCTC ATGATCTGCC CGCCTCAGCC

TCCCAAAGTG CTGGGATTAC AGGCATGAGC CACCGCGCCA GGCCTCAGCT GTTCTCTTTT

FIGURE 6 (11)

TACCTGCTGG GATGGCTAGT TTTCTGTGTC AACTTGACTG GGCCATGGGA TGTCCAGATA

TGTAATTAAA CAGTATTTCT GGGTGTTTCT GTGAGGGTGT CTTCAGAAGA GATTTGCATT

TGAATTGGTG AACTAAGTAA AGCAGAGGGC CCTGTCTAGT AGGGGTAGGC ATCATCCAGT

CTGTTGAGGA CTTGAATAGA ACAAAAGGCA GGGGAAGGTT GGAATTGCCC CCTCTCTGCT

TGAGCTGAGA CATCTATCCT GCCCTTGGCA CTCCTGGTTC TCAGGGGTTC AGACCTGGAT

TCCTGGTCTC CACCTTGCCC ATGGCAGACT GTGGGACTTC TCAGCCTCCT ATCTAATTAA

TAAATCTCTT CATACACACA CACACACACA CACACACACA CACACACACA CACACACACA

CCCTATGTAT CCTTCTGTTT CTCTGCAGAA CCATATCTAA TACACCTGCT TTTATGACGA

TTACCTATCG ATTCTGTATT CTGCCAAAAC TGAAAACAGT TCATTTTTCC ATCTCTTCTC

AGAGAGGCTT GTCAGCCATT AGTTCTCTGA TGGGCTCAAG AAGTTATGCA GTTTTTTTTT

TCTCACTGTT AGGATGGAAT TGATATTCTG TTGAAACTTT CTATACCTAA GTGGAAACTT

FIGURE 6 (12)

GTTTTGAGGT TATTTTCTCT ACTTACTTTT GCTGGAAATG GAACACTCTG TATCTAGTTA

AGACACATAA ACTGACTTGT GATACCATAA TGTTGTGTTG AATTTTATAT TCTTAGAAAA

TCATCTGTCA AGGTGTTAAC TAATGGCAAA GCATTTAATA AATCAGCATT CATGTATTCA

GGTGCTCTGA ATTATCTGAC TTTTAAATTC TTACTTTATA AATGAGAAAA TTGGGGCATG

GAAAAGTTAA CTCTCCTAAC CCCGAATTAT TACATTATTA AGGACAGGAC TTAGAGGCCA

GATATCTTAA GTCATTAATA TTCTTTGGCT CACAGAATTG GCAGTATAAC CTAAAGGTAA

TAACTAGGTG ATTTTCTTTT ATATCAATTA AATATGTCAG TTTTCAAATA TTCATAAGTA

CCTACTGTGC AGGGAAAGAA CATGCCATAC AAAAGATGTA GTCCAGGCCT TTAAGAAACT

TTCATTTAAT GGGAACTCAA GAAGTGTACA TATAAGGAGG GAAGTAGCAG TATGGTACAA

GATAATACAT ACATATCAGT GAATGATATT GCCAAAAAGT GCTATTGATA GAGAAATAAT

TCATTTCTGC AAACAGCTGC TGATCTCCTA CTGAAAACAG AGGAGGGAGA ACAGGACGCC

FIGURE 6 (13)

TCGTGGTCAG GATAGAAGAG AAAGACCTTG AGTTGAGCCT TGAACAGTAT TTAATATTCA

AAAGGTTAAG AGAGGAGAGC AATTGAGGAG GGGAGAATAG TTCCAGCACA AATGATGGTG

TACAAGATGA ACACAGTCAG TAAAGAGCAG ACTGGTCTGG ATGGAGAGGA GGATTTGCAT

CATTTGGGAT TACGTCATTT AGACCCTTGA AAGCCAGGAT TGAGTAAAGC CACAGTGAAG

CGACTGGCTC GTATGGAAGC TTTATTTTAA GAAGATTAAT CTGGTAGTGA CATGTGCCAA

AAACTGAATA GGTAGAAATG AGATGCAGAG AGCCCAGTTA GAACTAAGTC TGGTGCAGTA

ATGCAGGATT GAGGCAATAA ACACCAAACT ACAGTATCAC CAGATAATGG ATGTTTGAAC

GGACGGTTTA AAGGAAAATT GATGGTATTT GGTAATTTAT TAGATAATCC AGGGCCATGG

AATGAGAGGG GAAAATGACT AACCATAGTC ATCAAATGGT TTTTCTTAAT GAATCTGAAT

TTTGGTGTAA GAGCAACATT TTCTTAGGCC TTGCCTAGTT GGTACAGCTG ACTATGATAA

TGACTGCTAC CATGCTTGTT CCTCTTTTAG CAGCTGTGAG TCCCCCACCA GCCAAACAAT

FIGURE 6 (14)

```
GAGCCTCTTG AAAAGGACGA TGCCTTTTCA CTTCTCTCCA AGTGCTTGGC AAATAGGAGG
CCTTTTGAAG TTACTTTATA GTTAGGGGTT CCCAGTGAGT ATTTGAAATA TTAAGTCATG
CCCGTGGTTG ACAGCATGGC CCTACTGCTC ATCATCAGCT ATTAACCTTA GGCAAGTTAA
TGAACTTTTC TAAGCCCCAG TCTACTCATT TATAAAGTGG GATTATTAAT AATGTCTACT
TCATAAAATT ATGAAGCCTG AGTTAGGTCA TTCAGATAGT GTTTAGTCTG ATTCTTCGAA
CCTAGTAAAC AGTCAGTAAA CAGAAGCAAA TGCCACATGC CTGATTTATA TCCAAGGGGA
GAAAGGTAAA AGTGAAATTT TCATGATTTA TGGATTCAAA TTATACATTT CAAAGATGCT
TTATAAGCTA TTGTTTTGGT AAGAAGAATT GAGCTGAAAC AGAATTTTCT GACAGCAGTG
ATTATTAAAT GGTGAAATAG GCTATTGATG TCTTTAGAGG ATATAGATGT TCACCTTTTG
CATATAAGTG CACAAAAATT CACTAAGTAG ATATGTCTGT CTACACAGAG AGAGAGAGCG
TGAGAGCATT AAAGTTAGTA AACATCCCCC TCGCTTTTTT TTTTTTGAGA CAGGGTCTTA
```

FIGURE 6 (15)

CTCTGTTGCC TAGGCTGGAG TGCAGTGGTG CAATCGTGGC TCACTGCAGT CTCAACATCC

TGGGCTCAAG CGATCCTCTC GCTCAGCCTC CTGAGTAGCT GAGGTGTGCA CCACCACACC

CGGCTAATTT TTAAATTTTT TTATTGTAAA GGTGAGGTTT CACCATGTTG CCCAGGTCTC

AAACTCCTGA GCTCAAGCAA TCTGCTCACT TCAGCCTCCA AAAATGCTGG GATTACAGGC

GTGAGCCACC ACGCCTGGCC AGTAAACCCC ATTCATTTAC ATCATCTTAC TTGTCCCTCC

AAAATCCTGC AAAGTAGGTA GGTTCTGTCT TTATTTGTTA TTTAGGTGAA GAACTTGAAG

TGGTGTTGAG GAATAGGTGT TTTGCCAAGA GTCACGCAGC TGGAGTGGCA GAGCTGTATA

CTCTTCTGAT TCCACCAACG CTGTTTACAT CACATCTGGA GAAAAGTGCT CTGAGGCACA

GATGTTTAGT GGGAGGGATG AGACACAGGC TGCAATGCCT AAAGATAATC GGGAATAAAA

GCAGAAAACA AGACGTTTGT TTCTGTTAAA ATGAGACAGA AAATAAGGCG TTTGTTGTTT

GGGATTGAGC ACTTGGAGAA GTGGGGAGCG ATTTGATTTG GGTGAGACTG CTCCTGGAAT

FIGURE 6 (16)

GCTGCATCTG GTTCTGGACT ACTCATTACT AGGCTTATAG AAACTAGCTG GAGGAGGTTC

AAAGAAAAGC TCCAAAATGA TTAGCGGGCT GACGGGATTG ATTTATAAGA AATATTAAAA

GAATTAAATG TGTATAGCTC AGCTAAGCAA AGATGAAAGA GACCAGCTAA ATGTATACAA

ATATCTGAAA CGTGCAAACT TTAAAAAGAG AGATTAATTA TTTAACATGA TACACGGGGG

CACAATATGC AGTCACAGGA TGAAAATTTC AGCTGAGTAT CTAGAAGAAT TCCCCGATAG

TGAATCTGTT AAGGCTGTCT GTAGTGTGGC CTTTCCCTGG AGAGGCAATA GAAATTTCAA

GTCTTACGAT TTTAAAAGTT TCTTGGGAAC TAGGTATTAG ATGATGTTAG AGAATTATTA

TTAATTTGGT CAGGTATGAT AATGGTATTG TAGTTCTATA AGAAAAATTG TATTTTTTAG

AGTTACATAC CCTGAAATAT AAGCATAGAA TATGATGTAG GAGATTTGCT TTAAAATACC

ACAGTAAGGA AAGAAAGGAA GGAGGAAGAA AAGAAAGGAA GGGGAAGAAA GGGAAAAAGA

GGCAAAGAAG GAAGAGAAGG TAAGAGAAAG AAAAAGAATG AAGGAAGAAG GCTGGGCACT

FIGURE 6 (17)

GTGGCTCATG CCTATAATCC CAGCATTTAG GAGGCCAAGT TGGGAGGATC ACTTAATTAA

GCCCAGGAGT TCAAGGCTGC AGTGAGCTGT GATTGCGCCA CTGCACTCCA GCCTGGGTGG

CAGAGTGAAG CCCTGTCTCT AAAAAAAAAA AATAAGTTAA AAAGAAAGAA AAGGATAGAT

GAAGTATGGC AAGATGTTGG TAATGTTGAA CCTGAAGGAA GTTAATATGT GAGTTCACTT

TCCTCTTCAG TCTTCTTTAT GTATGTTTGC CAACTTTCAT AATAAACAAT TTAAATTATA

TTTTCCTGAT CAAAACTTAG TAGCAGTATT AATCCCTGGG CTTCCTGACT AGAACAGCCT

CATTACCACA TGGGCAGAGT TCTGGCCGAC CAGGGACCAC GTAGTGGTTC ACCATCTTGC

TCTGGTAATG TGGTCTGGGC TGAAGGGCCC TTTCTAAGGT TGTAGATAGA AATCCAGGAA

ACTTGTTAGA ACTGCAGACC TATCAGGGTA CCTGCAGGAG GTGAGTCTAC TAAGGTGAAA

AAGCAGAGGG CAGAGGTCGT GATTAGCAGC TGACCGCCCC CTGCTTTTCT GTCCCTCATT

CGTGGAAAAT TGAGTGGAGC TCAATTTTGA GTGGAGCTCT AAGTAGCTCC ACTTGTAGAC

FIGURE 6 (18)

ATTGAGTGGA GCTCTAAGTG TCTTCAGAAT AGCAAAACAC TAGTTTTCTT TTTCTTTTCT

TTTTTTTTTT TTTTGGAGAC AGAGTCTTGG TCTGTCGCCC AGGCTGGAGT GCAATGGCAC

GATCTCCGCT CACTGAACTC TGCCTCCCGG GTTCAAGCGA CTCTCCTGCC TCAGCCTCCC

GAGTAGCTGG GATTACAGGT GCCCACCACC ACGCCCAGCT AATTTTCCTA TTTTTAGTAG

AGATGAGGTT TCACCGTGTT GGCCAGGCTG GTCTCAAACT CCTGGCCTCA AGTGATCCGC

CTGCCTTGGC CTCCCAAAGT CCTGGGATTA CAGGTGTGAG CCACCACACC CAGCTGCAAA

ACCCTATTTT TCTTGAATGG AGAAACACTT TCCCCTTATT TATTGAGTTT GGGAAGCAAG

AAGAGGGGTA ATTCATTAAG TGAAAATTTC CAAAATCCAG AAAACATCGA TAAAGCAGCA

GCTTAATTTT TTTAAGGAAG AATTTTTTAA ACTATCTTCT TTTGAGCCTC TTTAGGAAGA

CCTCACGTCC TTGCCTTGAA TGTTGAGAGT GGGAAATCCA GGGAGTTTTG GAATGCATGC

CTTATGTCTG CTTTTTTGTT TGTTAGAGAA ATATAAATAT TTTATCTAGG TTTTGCTGAT

FIGURE 6 (19)

GGCAGTCAAG CATGAACACA ACCCACTGTT TGAGAAGCTG TAATTTCTGA ATTTCTGCAG

AGTGCACATC TAGGCCAGCA AATGGCAGTA AGAGTGAGGT GGATTTAGCT CAGTGTAAGG

ATGAACTCCA GAACCATCGG CTCTGACTGA AAGTGAAGCG GCAGCCGCGT TGTGGGAAAG

CTGGCTGGAG TCTCTCTCAT AAGCAGGCAT TCTTTTTCTC CAGCCCGTCA CTGTGTTGGT

TTGGGCCCAC GGTAAGCCTC CTGGCCTCTA GGCTGTAACC CCCACCATCC TCCTCTGCCT

CGCCTCCAGA GTGATTGTTC TGAAGCACAA CTGGATGTCA TTCCCCTTCC TGAACTCCTA

GCACCTACAG GGACTCCATC CCTTGTGCCC CACATACCTC ACACGTAGAC ATTCCTAATG

AAGATTTGAT TGAATTATTG TAAACTCAGT GCCTCCCACT CTTCTAGTTG CCTCTCTGCC

TGCCTTTGTA CATTTATTTA TTTATTTATT TATTTATTTA TTTATGAGAC AGAGTCTTAC

TGTATCACCC AGGCTGGAGT TTAGTGGCAC CATCTCAGCT CACTGCAACT TACCTCCCAG

ATCAAGCAAT CCTCCCACCT CAGCCTCCCG AGGAGCTGGG ACCATAGGCA CGTGCCATAT

FIGURE 6 (20)

GCCCGGTTAA TTTATTGTAA TTTTTGTAGA GATGGGGTTT CATCGTGTTG CCCAGGCTAG

TCTTGAACTC CTGGACTCAG GCGATTCGCC CGTCTCAGTC TCCCAAAGTG CTGGGATTAT

AGGCGTGAGC CACCATGCCC AGCCGCTAGC ACTCATCTTA ATCGTATATT TACTTATCTG

GCTTTCCCAC CAGACTGCGG GCTCTTCAAG AGTAAATGCC ATGTTTTCAC CTTTATTTCC

CCAGTTTGTG GCACATTCTA GGCACTCGCC ATCATGAAAT AAACCTCTGG AGCTGTGATA

TTACAAACGT GGAAAGATGA CGAGCACTCA GCAACTTTCA GTGAGTAAAC AAAGGCTTTC

ATTCAGCATG ATTTATTGAC TGCCCAAATC TGGGCTGCTT CCTGTCTGTG GTTCAAGGAG

AGCATAGTCT ACAGAACCAG AGACCTGGCT ACTCTGGAAG TTAGACTTAA GCCCACCCCG

GTCCTTGAAT GGGGAAATAT TTCCCTTCAT TCCTGTGTTT TAGGGACAGA AAGATGAGTA

ATGCAGTGAT ACATGCTGGA AATGTTTATT CCACTACCCG AAGCTGCCTC TCAACTTAAC

AATCCATGAA AGAAACAAGA TGGTATATAA CTTTTTCTAA TTTGTGATGC CTTTGTTTAT

FIGURE 6 (21)

TTGTTTCCGG TTAAAAGAGG AGGTGGCATT GAATTGTTTG TTTGGTTTGG TTTCTTCTTC

AATAAGAAGC ATCTTAATAT AACTAGACTG GACATCTGTC CCATTTTCAA AAATTACAAG

TTTCGATCAT TGCTAAATTG TACAGATCCC AATCTGTCTG CTCTGCATAC ATTTGCATTT

ATAAAAGCAG AAGCAGACTA GCAGTCTTTC TAATGCAATC CCCCAAATGC ATGAAGTATT

AGATTGCTTC TCCCTATTGG TTCATGCATT GCTAAAGGCT TAAAAGGATC ATTGATTTTA

ATTATTTAAT GTGTACAGCA GGCTGAGCTT CCTTTCTTTT TTAAGGGAAG AACCTTCAGG

GGCATTGCTT TAGTTTTTTA ATGTTAAATC TCATTTTTCT TTGAAAATAA GAAGTTAAAG

CTGTATTCAC ACAAGCTCTC AAAGTGCCAG ATTTTCATTG TGTTTTTAAA CCATCTAGGA

AATGTTTGAT TCTAATGAAA CATTACTGCT GAAAATTGGG CTGAAATTGC TGGGCTGGAA

ATATTGTTAT AACTTCACAT GATTCCAGTG TTGTATTATT ATTTTTTCTT TTTCTTTTTT

TGACCCGATA TAGATGAAGC GAAGAGACAA GGAGCAATCC CATGTGTAAT AGAAAAAGGC

FIGURE 6 (22)

AGCCTGAATT GTTGTTGCTG TTTTTGAAAT TTAAGCTGGT TTTCGATTAA ATTCAGTAAA

TGGTCCAGGA CTATAAATGT TGAACATTTT TTACCGTGTG ATTTAAATTT TAGTCTTATT

GTTTTTTTTT TTTTTGATGG TTTACATTTT CCCCATGGGA AGCAGCTATG TCATGTCGGC

ATGATTCATC ATGGTAACAT CTCGGGTTAT TTTGGTTTGT GTTATGTTCA GAAAGCGGAA

TGCCAAAAAT AAAGAGTGGT TTGTGATGTC TAGTGTGTCT TCCTTTAACA AATCAAAGGC

TTTTATTTAA TCCACTTAAT GGGACACTGC AGAAATTTAA AAAATGGAAG TCCCATCCAC

AGAAGGCAGG TACTATGATG TAAAAAGTTT AGGTGGGGGA TTAATAGAGT GATCATATAA

TTTATGAGCT AAACCGGAGG CACTTTTTTT TTTGAGATCG AGTCTCACTG TTGCCTAGGC

TGGAGTGCAG TGACGTGATC ACAGCTCACT GCAACCTCCG CCTCCCGGGT TCAAGCGATT

CTCATGCCTC AGCCTCCTGA GTAGCTGGGA CTATAGGCGC CCACCACCAT GCCCAGCTAA

TTTTTGTGTT TTTTGTAGAG ATGGGGTTTC ACCATGTTGG CCAGGCTTGT CTCAAACTCC

35/285	46/285
36/285	47/285
37/285	48/285
38/285	49/285
39/285	50/285
40/285	51/285
41/285	52/285
42/285	53/285
43/285	54/285
44/285	55/285
45/285	56/285

FIGURE 6 (23)

TGACCTCAGG TGATCCGCCC ACCTCGACCT CCTAAACTGC TGGGATTACA GGCGTAAGCC

ACCATGCCTG GCCCAGAGAC ACTTTTGAGA GTGAAGAGGA AGCTGAGAAT AATTCACTGA

TCTACAACTG GGACCATCCA GGGCAAGCCA GATGCCATTA CCACTAGCTA GAAAGCTTGC

CAAGGTCTCA TTTACCTTGG TATATAGCAA ATTCTTCTTT TGAATTCTGG AAATTCTGGT

AAGTCATTGA GGTAGCTCTG TGCCAAGGAG CAATATGGTA GAATTCTAAT ATTTCAGGCA

GACAACACTT TCCTGCATTT GTAGCAGGTA AAGGGAGGTC AGGGCAGAAG ACAAAACCAC

TGGGACTCGA CAAAGGGCAT AAACGTCTAA TGCACCTGAT GTAGCTGATG GTAAATTGTT

ATCAGCTAAA GATCTTTCAT AATAAATAAA CTTATCATTT GTAGGAGGGC ACAGAAATCG

TGGAAAGCTG GGATTCAGGT TGCCTGTGGC TTTAATTCTG GAATCAGAAA TATTAGTCAA

GGATATCAGT CTATGAAGTA AGTTTTCAAT GTTATATGCC ACAAGATGCA GCTGTCCTAT

TTTCACTTCC AGTAATTCCT TCTGAATTAA TACACCTTAA AAATAGCTGC AGCTTCTCAA

FIGURE 6 (24)

ATCTGTGAGA ATCGTATGTG CTGCTTGCTA CACTTTCTTT TTCCTGAAGG CTCTTTGAGG

TCTTTCAAGA ACTCAATTCA ATTCAGCAAC AATTAGGGGG TCTAAGGTAT ACAGACGCTG

TGCAAGATGC TCCTGAGACA CAAAGAGGAG GTCAAGCCCC TGCCTTCAGG CACCTCTCTA

TAATATAGGA GGAGAAAGAG AAGAAACACT AATACACATA GGTAGGTGCC ATTAAAAGGG

TACATACATT AAAGCCAGGT GGTAGGTGTA AGAAGATTTG TAACATGAGA ATTTTCTGCA

TGTTTGAAAT ATCTTATAAT TTTTAAAAAT TAAAATGGGA GATACATATA TATGTATTTA

TGTATGTATA TATGTATGTA CATATACACA CATATATACA TAAATATATA CATAAATATG

TATATATGTG TATATAGACA TAAATATGTA TATATGTGTA TATATACATA AATATGTATA

TATGTGTATA TAGACATAAA TATGTATATA TGTGTATATA GACATAAATA TGTATATATG

TGTATATAGA CATAAATATG TATATATGTG TATATAGACA TAAATATGTA TATATGTGTA

TATAGACATA AATATGTATA TATGTGTATA TAGACATAAA TATGTATATA TGTGTATATA

FIGURE 6 (25)

GACATAAATA TGTATATATG TGTATATAGA CATAAATATG TATATATGTG TATATAGACA

TAAATATGTA TATATGTGTA TATAGACATA AATATGTATA TATGTGTATA TAGACATAAA

TATGTATATA TGTGTATATA GACATAAATA TGTATATATG TGTATATAGA CATAAATATG

TATATATGTT GTATATAGAC ATAAATATGT ATATATGTGT GTATATAATA ATGTGTGTCA

TATACACACA TATATACATA CATAAACATT CTGCATTATA CCATTCACTT TGTAACCCAT

CTTCCCTAAA AACTGTCTCA TAAAGAGTCT TCTTTTCCCT GTACCTATGC AATGGTAAGT

AGCAAAACAC ACATTCTTTT GGGTCCCCAT AACATTCCCT GTAGTTTGCC CTTAACAGTC

TTTGATGTGA AATTTACTGT TTCTGTCTTA ACCTTGCCTG TCTCGCGTAC ATGGAGTTTT

GGCTCCTGGC TCCTAGTCTG CATCTTCACC CCATCCCTTG CCCAAAGAAT CTGGTTATGT

GACCACTGCT CATCTTTTCT GCTGCCACAA CTCCAGTCCA AGCCACAAAC CTCTCTCTCC

TGGACTCCTG CGGGGAGTTC CTTTCTCTCC CTGCATGAGT CTATTCTCCG CACAACTGGC

FIGURE 6 (26)

ATAGGTAAGT GAGACTGCGG AAGAGGCAAG TTTGCAAGTC CAGAGGAAAT GAAGACTCTG

CTTGTGCACA TGCTGGGTTT GACGGGTGCT GGATATCCGA TGGATGGCCC TTAAGGTGAG

CTCAAGGCTT AAGGGAGAGA TAGGGGCTGA TGATCTGAGA TTCATCAGTG TGTGGCTGAT

GTTTAAACCC AGGGGACAGG ATAAGAAGGT TATTCCAGGG AGAGCGTAGA TAAAGAAGCT

AAATGGCTTC TGGGTCCTTA GTCATTCAAA ATCGGACCTC TGAGGCAGGA GGAAAGCCCA

GAAAGAGTAG ATTCCTGGGA CTCACGGGAT AAAGACTTTC AAAAAGTGGG GGCTGGCCAG

TGCTGCTGAA GGAAGTAGCA GGACCGGAAC AGAAGGGTAA TCGTTGGACC TGGAGAACTT

GAATTTGAAT TTTAAGGTTG GTAACCTTAA AAAAGAGCAA TTTTAGATAC CTTTTGAAAT

TATTTGCAAG ATTTGTTTGG TATATGTGTT ATTCCAGGCA AAGGGACCAG AAAAGTAAAA

AATACTTACT GAACAGTTAC TGCATGCCTG GCACTGTAAC ACCCTGTTTA ATTCTCACGG

CAACCCTATA GAGTAGGTGT CATCATCCCC ATCTTACAGA TGAGGATATG AGGTGCAGCT

FIGURE 6 (27)

AGATTAAGCA GTTTGCCTCA GGTTACACCA ACTGGTTAAC GTAGAGCTAG GATTTGAACC

CGGATGGGCT GATCCCAGAG CTCATGCTTT AAATCGCTAG ACTGGTGCTC ACAGAAGACT

GGGACCGAAA AAAATTAATA AAAAAAATAA GGAGCCCCCT GGGCTAGCAA ATTAGGAGTT

GTTCAGACAG ATGTGAAAAG GAAAGCAAGG CAGAGGGAAA GTCACTGTAC AGAAGAGAGA

GACCCATGAC AGCAGAGACA GTGAGCTGGT AAAGTGGCTG GCGATCTAGC CCCTGAAAAT

ACCTCCAGAG AGGCAGGCTC ACGCCTGTAA TCCCAGCACT TTGGGAGGCC GAGGTGGGCA

GATCACCTGA GGTCAGGAGT TTGAGACCAG CCTGGCCAAT GGCGAAATCC CGTCTCTACT

AAAAATACAA AAATTAGCCG AGCATGGTGA CAGGCACCTG TAATCCCAGC TGTTCAGTTG

GCTGAGTCAG GAGAATAGCC TGGATCCGGG AAGTGGAGGT TGTAGTAAGC CAAGATTGCG

CCACTGCATG CCAGCCTGGG CGACAGAGCA AGACTTTTCT TAAAACAAAC AAACAAAAAA

GAAAAAAGAA AAGGAAAGAA GAAAGAGACA AAGAAAGAAA GAGAGAAGGA AAGAAAGGAA

FIGURE 6 (28)

GGAAGGAAGA GAAGGAAGGA AGGAAAGAAA GAAAAGGAAA GAAAGAAAAA GAAAGAAGAA

AGAAAGGAAA GAAAAGAAAG AAAAAGAAAG AAAGAAAATA CCTCCAGAGA GCCAGGTCTC

TTAGGCCTTC TGAGAAACTC ACATCCCTTT TGATGAACAC AAATGCTTCA CACTCTCAAT

GTTATTGGTA ATCCAAGTTA TCAATATACC TAAATCACTT AGTACTGAAT CTGGCATATA

GTAATCACCT AATGAAGAGA TAAGAGTCAT GGAGTATTCT GAAGCAATTA GAATCAATAG

ACTCAATATA CACATGGCAA CAAAGTTGGA TCTTAAAAAC CGACCTGAGT GAAAAAGGAA

AGGGAAAGAT ACATAACACG GTACCATTAT GTAAATTGAT AATATATGCT TACACAATTT

GTAAGAACAC ATACAAATAG ATACATGTAT ATTAAATATA CTCGAACGGT TACCTATGGG

GTGGTGGCTG GAGTGGGGGT AAGTCCGTAA GCTGTAATGG AACCTAAACA AATACATGAA

ACGAGTAGGA ATCAGAAGGA GTAACAATAA AAATGTGCCA TGAACTGAGG AGTGTAAATT

AATCAACTCA CTGCATCTGA GGTTAAAAAT AGAAAGATGA TAATTGTTAT TCTTATTACT

FIGURE 6 (29)

CGTAGGTCTT CCACTTGCAC TCAGCTTTAC AATGTTGGAC TATCCTTCAG ATGGCACCCT

CCTTGCACTT GCTCAGGCAG GAGAGCTTTT TCCTCCAGCT TTCTAGGTGA TTTAATATAT

CAGGGAATAA GTATAAAAAA AGGCACGGTG CTCCCTGGGT AGCCTTTCTG GACTTCAGAG

CTAAATTGCA AAGTCAGTTT TACACATGTG ATTTCATCTA TGAAATTAGG GCAAGGTAGA

AAACTGGCAC AGAAAAAATG TGATTTATTA TGGTGTTACT ATCCCTTACA AGCGGAGTGT

CAGCTGCCTC TTTTTGTCCA CTGATTTAAG GCAAGATGAA CTGAAAGTGG CTATGATCAC

GTCTTCAAAA GCACACTCTG GCCCCTCGGC TGCAGGCGCC CTGCACATTC CCCAGCTGCG

TGTCCGGTGG TGACACAGTG CATAATTGTG GCGCCTTCCT GGTGCAAACT GTCTCACTTA

GCTCCGTCTT GCTGGCACAG CAGAAAGGAA GAAATCGAAA ATGTTTGGAT TTCAAAGGTA

ACAAGAAGCT GGAAAACAAC TACTGGCCGA GTCTGAGAGT TTCAGCGGAG ACTGGTGCAG

CCTTGTGTTT TTCCACTGAC AGCTGAAAAT GAGCCCAGCT TCAGTGAAGC TTGTTTCCTT

FIGURE 6 (30)

CCCTCCTCAA GGTTACCCAC AATTCTCAGT TCTCTCAGGA AAGCCAAAAA ATGAATTTGA

GGGTTTAGGA TTGTGGTTCT TTTATCTATT ACAGGATTGA TAATATGTTC CTCCACCAGA

TGTTCTGCTT GTAACAATAC TCACTTCCTG ACACTACTGC ATATGCAGGA GTGTTACTAC

CAAGGTAAAC ACAGAATTGG CTGCCCAATT CCAAATCCCT GAACTGAGTG AGAGAAATCA

GAATTATAAT AGGGGATTCA ACAGAGCTGG CTACGGATGT GCCAGTGGTC AGATACTTTG

CTCATCATAC GCAGGTGCTG CTGCTCTAGC AACTGCTCAC TGCTTCATTT CCTGCCTTGG

TCTTTAAATA CTGCTTTTCT CAGCTCAATT GGCTTTCTTC CCTCTGGCAG TCACGTTTCT

TTGGGTCAAA CAGCAAATGA TTCTTTAGAA TCACCTGGTA CTCAAAGGAG CTACAAGACA

TTGGGCATCC ACTTCCACTC TCTTGGAAAA ACAATTTTAT GGAAGCCAAG GTTGCCATAG

TGCCTCTTGA GGTTGTTTGC TCAGCCAAGG CCCAAGCTTT GTGCTTCAAA CATGAAATTA

GAGAGCTTCA GAACAAGATC CACATTTTCA ATGGCCTCAC CCAACTGGAT AAAAGAACAA

FIGURE 6 (31)

```
TTGCCATATC TCAATGACCA CCTTTTTCAG GTGGGATGGT AGATGCTGGA ATGGGTCACA
GCATTGCCCA ACCAAACTTT GCAAAAAAGG CTGGAAGCTC TGACTGGGGA CCCTAAATAT
GCAAAAGTTG ATAGGCTCTT CATGCAGAAT ATGAACCCCG TGTATGGATA TAGCTAAAGG
GTTGGCCTTT ATGTTTCTAT TCCTTCACAA ACCTGGTAGA ATAGATATGC TTGTTTCCCT
TTAAAAAATG TCAACAATTG CATTTATGAT GCTGTGTATA GTAACTCACA GATCATGCTC
CATGAAAATG CTTCAGAACC CAATATAAGG AGATTTTTTA GCCATGTGTG ACAAAAGAGA
GGCCATTTCA GTGTTGAAAT TGTTCAGAGA AGTATTTGAT TATGTTTTCT CAGATCTTTT
TATTTTTATT TTTTTTGAAA CAGAGTCTCA CTTTGTCACC CAGGCTGGAG TACAGTGGCT
GTGGTCTCGG CTCACTGCAA CCTCTGCCTC CCAGGTTCAA GCGATTCTCC TGTCAGCTTC
CCGAATAGCT GGGATTACAG GCGCATGCAC CACCATGCCT AATTTTTGTA TTTTTAGTAG
AGACAGAGTT TCGCCATGTT GACCAGGCTT GCCTTGAACT CCTGACTTCA GGTGATCCAC
```

FIGURE 6 (32)

CCACCTCAGC CTCCCAAAGC ACTGGGATTA CAGGCATGAG CCACCGTGCC CAGCCTGTTT

TCTCAGATCC TGTATTTGTT TCTGAAGCCT TCATTTCTAT CTTCTTATTC ATTTTGGAAG

TAGTACACCT AAGTAAGGTT TTTAACAATC AAATATCTTT GGAAAATTCC CTGGTTCCTT

TCTTATTCCT ACAAAAATAT GTTCAGTATA GCTGATGTTA TGTTTCTTTC AAATTATTCA

TTTCTCTATC TCAGAATTTA TCTCATGCCT AATTGTTATT GAATAGTCTT CACTTCTTGT

CATCCAGTTT CTGGTCTCTT ATTTCACTCT AAGTCTAAGT GGCTATTAGA ATAAAGAGCT

TGTAACAGAT TCTTTCTCCA ATATGTCTTA TCTTTTGACT GCATGCCAGT GACAAACTGT

TAACTGTTTT GATTCTTCAT AACATTCCAC AGAACATGCT GACTCCTCTC TTCCTGAAAG

CAATGCCCAA GCACAGCATT GTTAGATAGT ATGTACGCAA CAGGGACATG GGTGCATAGC

AAAAACTAGA AGGAAGGAGG ACCTTCCTTA GCAATGGGTG ATATGGTCCC TGGACTTAGA

CTCCAAAGGG TCGTGAGGTG AAACACACAT CGTCCATACC CAGGAAGCAC ACAGGTGGGA

FIGURE 6 (33)

TGGAAGAGCT GTGCCTAATG AAACTTCATC CACGTGGAGG TGGAGGAGGC TGCAGCTGCA

AGAACTCAGA GCTGCCTTAC CCAGACCAGG GACCAGGGAG GGCTTTCTGG AGGAAACAGC

CTCTGAACTG CCAGCTGATA GAGGAGCTCT ACCTCAACTC TTCTGGTTCC CCAGGGCTGC

TTTTCCACGT CCATTTATTG GCACTGAAGT TTGAATACCT TCAGGGGCCC GAAAGCCTGC

CAGGTCCTCT TCTCTGCAGA GCAATCACAC CAACCTGCAA AGGGCTAGGA AAGGGCTGTC

ATCATCTCCT ACTCAGAAAC TGGTTCACTG GAAGGACTCA GGGGCCACTG AATACATCCT

GGCAGCTTTC ACAAGAAGGG CTTCTGACTC AAGGATGTTT CCATCTTTGC CAGGTCGCCT

TTTCTCCTTC TCTTAGAGTT TGGAGGACGC AAATGTGCTG AGAAGTCAAC CTTTCCTGCA

AGGTGAGACA CAAGGGCCTT TCCCAGCAGA AAGAAGAGAG CAAATGGAAG GTCCTTCTTC

CTCCAGTAGA GGATGGACTC TGTCTGGCAG CCACCCAACA GGAAAAGCAC AATGCATGCC

TGCCTGCTTC CCTCCCTCCC TCCGTTTCTC CCTCCCTCCC TCCTTCCTCC CTTCCATTCT

FIGURE 6 (34)

```
CTTCCCTTCC CCTCCCTTCC CTTCCCCTCC CTTCCCTTCC CCTCCCCTCC CCTTCCCTTC
TCCCTCTCCT TCCCTTCCTC TTCCCTTCCT TCCTCTTCCC TTCCTTTCCC CTCCCCTTCC
TTTCCCTTCC TCCCTCCCTT CCTCCCTTCT TTCCTTCCCT TCTTTCCTTC CTCATTTCCT
CCCTTCCTTC CTTCCTTCCT TCCTTTCTTC CTACTTTCCT ACCTTTAGGG CTCTGTGTCT
TTGGAGTCCA TTCTGATTAT GCTGTAATGT CTGCCCCTTC CTCTTCTCTG TCAAAAAATG
AAAGACATGG AAGCCACTTG CCTTTTACTG AATTAAAAAT TAGTAAAAGA GCTAAAAATT
AATGGTTAAA AATGTACGCA TAAATTATGC AGTATACTAA CCAATGAAAA GATACACTTC
TCTTAATTAA AAGCTGACAG GGAGGGAAAC AAGAAAAGAG AAACACAAAA CAATAATCTA
AATGACCTAT TAGTTGGAAG AACAACATCA GAGAAAATAG ATACTGTGTA TAGTCATGTG
TATGTCTATG GAATAACATT TGTAGAGAAA TCTGGACTGA TCCTTTCTGA GTAAAGAGAG
CTGTGGGTAC AATTAAGGGG AGATTGAAAG GAATCCAAAA GCATAGCAGA TGCTGTGCCT
```

FIGURE 6 (35)

CACTGGAATG GTTGCCGATC TCCTCCAAAC TATGAAGTGT TTGAGGCTCA ACTTTAATAT

AATTAAGATA CAAAGACAGA ATGAGAGAAA GAGAGAAGGG AGCTCACTGG AAGAACACTC

AAGATTCCTT ACTACTCATT CTCTAAAATT ACAATTGTTC TAGATGGAAA AGAAAAAAAG

CTTCTCTGTT AAAAAAGGAG CTTGTGCTAT AGGAGGTTTA AAATATACTT CTGACCCATC

TCCAACATTC TAAATCCTTC CCAGAAAAGT ATGCCAATCC CAAGAAATAT TCAATCAAAT

TGCTGGAAAG AAAAATACAA AATATTAAAA TGTATTAGGA AGCGACAGTA ATTAAATCAG

AACTGGAGCA GGAATAGACC AGCAGATCAA TGAGACAGAC ATCAAGTCCC GGAATGTGGA

CTTGCAAATG CATTAAGTAA TATGATATGC AATAAAGGTG GCACAGTGAA CCAATGGGAA

AAAAATTAAT CTTATAATAA TTGATATTGC AATAATTGTC TAGTAATTGG GGGAAGAAAT

AAGCTTATTC CTTATCTCAT TTCTTTTTTT CTTTTTGAGA CAGAGTCTCA CTCTGGTAGC

CCAGGCTGGA GTGCAGCGAT GCGATCTCTG CCCACTGCAA CCTTGCTCTC CCGGGCTCAG

FIGURE 6 (36)

GCGATTCTCC CACCTCAGCC TCCCGAGCAG CTGAACTACA GGCGTGTGCC ACCACTCCCG

GCAATTTTTT TTTCCATTTT TAGTAAAAAT GGGGTTTCAC CATGTTGCCT GGGCTGGTCT

TGAACTCCTG GGCTCAGGCA ATCCACCCGC CTTGGCCTCC CAAAGTGCTA GCATTACAGG

CATGAGCCAC CGCGCCTGGC AGCTCATTTC TTAGACTAAA TAAATTGGAG ATGGCTAAAA

GATTTCTATG TAGGCCAACT ATGTTTTTAA AAAGTTTTTT TTTTAAGGAT ATCTGCTGGA

ACCAATCATG CCACCAACCA AAGATGCAAG ACTATAAAAC ATACCCAGTT TTTCAAAGCA

TTTAAAAATT ATTCTAAAAA TATTTTTTCT CCAGAAATTT TGCATTGATT CCCTGAAGAA

GCATTAATAT GGGACCTGAC TTATAAAATG ATGAACTCAA TCTCCCCACT CAAGGTAGGA

GTCTCTCAGA TTTAAAAAAT AAGCATCCTA GTCCTCTTGT CCCTGTAAAA GTTAACCCTT

ACACCTGAAA CACCAGGAGA CTGGCGGTTG TTTGCATAGG GGTTACAATT AAAGTTGAGC

TACCTCTGAC ATCTATTAAC ACCAAAATTA GTAAACTATG CATGTATGGA GACTTTTATG

FIGURE 6 (37)

```
ATTGAACTTG TTTATTGAGT CAAGAGATAT AGTTTACAAT GAAAATTTGG GGCATATCAA
AATGACCTTG GCTTAGCTTA GCATTTGCTG ATGTTAACTA TTTTCTTCAT TGGGCTGATT
TTAGTTGCTT AGGAAAAATA CAAACACACA CACTTTAAAA TTATATTAAA ATCCCGTCCT
AAACCTCAGA GTCCAGAACC GCATCCTAAC ACTGGTCATG CATAATATGT TTAAATTTTT
GTGCTTTAAA AACTACAAAT AAGGAATGTA TTAATAGTTC CACAATCAAT GGTCAGTTAG
CCGAGGGAAG ATTAGCATAG TTAAAGACTT AAAATGGCTT TACAACATAT ATCAAAAGGA
CAAAATAAGG GGAACAGAGT CTAGAAATGA GGAAACTGGG ACACAGGCAA AAAAAAAAAA
TGAGAACTGG GACATGAATA ACGCAAGGGA TAAGACTAAT ACACAAAACA CCCCAAATAA
ATAGCCAGCA TTTGCTGAGC TCTTACTGTG AGCCTGTTCT AAGCACTTTA CATATATTAA
CTCATTTCAT CCTCAAGGAA CCATCTGAGG CAGGCACTGT TATCATCTCC ATTTTACAGA
TAAGGAATAG ACCCAGAGAG GCTGAGCAAC TGGGCCTATT CCACAGCTAC TATGGTGGAG
```

FIGURE 6 (38)

ATGAGATTTA AATCTAATCA TTGGCTCCAG AGCCCATGCA CCCAATGGCT GCACTAAGTG

AATGCATGCG CTATCAACGT TGCCAAAAGT GGGCCACAGC TCGGATCTGC GTTTTCCAGT

AGCCAAAGCA GAGAGTGTGA TCAGACCTCA CTTTAATAAG CAAGTCTCAA GCCAGAGAGA

GGTGGTATCA GGCAGCAAAC AGGCTGCTAG TCGAAATCCC ACTTCTTCTC TGAGTGGTCC

ATACAGTTTT ACTCTACTTG CTTACAGAAT GAAAATAGCT GGAGTTCAGG TGCGCTTTCA

ATGCCCTGTT GTCAGGATTG GGCTTTTCAA GTTTATTTTT TGTTGTTGTT TTTAATAGAC

TGTACTTTTT AGAAAATTTT TAGATTTACA GAAAGATTGA GAGGATAGTA CAGAGAGTTC

CCGTATACCT CACACCCAGT TTCTGCAATT ATTAACCTCT TACATTCATG CGGTACATTT

GTTACAATTA ATGAGCCAGG GCCGGCCGGG CACAGTGGTT CAGGCCCCTA ATCCCAGCAC

TTTGGGAGGC AGAGGCAAGC GAATCACTTG AGGTCAGGAG TTCGAGACTA GCCTGACCAA

CATGGTAAAC CCTTTCTGTA CTAAAAATAC AAAAAATTAG CCAGGCATGG TGCTGGTTGC

FIGURE 6 (39)

CTGTATTCCC AGATACTCAG GAGGCTGAGG CACAAGAATT GCTTGAACCA GGGAGGCGGA

GGTTGCAGTA AGCCGAGATC GTGCCACTGC ACTCCAGCCT GGGCAACAGA GCGAGACTCC

ATCAAAAAAA AAAAAAAAAA AAAAAGAAGG AAGGAAGGAA GGAAAATTAA TGAGCCAATA

TTGAGACATT ATTATTACTA AAGTCCATGC TTTATGCAGA TTTTCTTAGT TTTTACCTGC

TGTCATTTTT CAGTTCCAGG AATGCATTCA GGATGCCATA CCACATTTAG TTCTCATATC

TGCTTAGGCT CCTCTTGGCT AGACTGAGTT TTAATCTACT TTCTGCAGAG CCTGAGAACT

TTAGCATAAT TTCCTTGGAA ATTACAGCTC AATATTTTCA AGCACTTATA CAAACAGCCT

AATGTTACGT TGGCCCATAA CAGTGTTTCA AGGTAATAAA CTTCTTTGTT TTCTGTGCCG

ATTGAAAGAA CTGCTGCTTA GCCTCCTGCC AGATGATGAA CTGGGTACAC ACGAGCATTT

TTCCAGGTAA AGCATATTTC GTGCGACTTC TTAAGCTGCA GCCTTATATG CAATAATTGT

CCATTTACAA GACTTATGTT CGAATTTCAG GCACTCTGTT TTCACTAACC ATATCCTTCA

FIGURE 6 (40)

ACTTTGATAA GTACTGCTTT AATCAACTCA GAAAATTTAA CTTGACTAAT TTTTTTTCAC

CATCAGTTTT TTTTCTGTTG ACTCTTTCTC CTTTTTCTGT TTGCCCAGAA ACATGCTCAG

GATTCTCTCA GGCTTTAAAA AATGAAAAAA TGTTTCCTGC AATCTAGTTA CTCCTTGATT

CTCTTGTTCT GTTTATCGCT GGAATTCTTG AAAGCTTGGT GTATTAGTCT TTTTTCATGC

TGCTGATAAA GATATACCTG AGACTGGATA ATTTATAAAG AAAAAGAGGT TTAATGGACT

CACAGTTCCA CGTGGCTGAG GAAGCCTCAC AATCATGGTG GAAGGCAAAA GGCATGTCTT

ACATGGCAGC AGACAAGAGA GAATGAGAAC CAAGGGATTT CCCCTTATAA AACCATCAGA

TCTTGTGAGA CTTATTCACT ACCACAAGAA CAATATGGGG TAAACCGCCC CCATGATTCA

ATTATCTCCC ACCGGGGCCC TCCCACAACA CGTGGGAATT ATGGGAGCTA CAATTCAAGA

TGACATTTGG GTGGGGACAT GGCCAAACCA TATCACCTGG CCTATAGCAT TATTTCCATT

TCTTCCCCAT CCTTTTATTC CTCAAACCGG TACAACCAGA CCTCTTTTTT TTTTTTTCTA

FIGURE 6 (41)

CCTGAAACTG CTCTTTTGAG GGTAGCTGAT AAGTCCAAAA TACTGTCACC TTTTCTCAAT

TCCGTTCCTT CTTATGCCTT TGGAGCAATT GACTGTGTTG GTTGCCCCCT CCTTTAAAGT

GTCTCTCACT TGGTTTTATG ACTAATGATG ATTTTCTTTT TCCTCTCTAA ACATTCCGCT

ATCTTTTTAG CTTCCCTTCC CCCTCCCATC CCCTAAATGT CCTTGTTTCC CAGAATCTGC

CTCACCTCTT TGACTTCTCT ATGCCCTGTC ATTCACTCAT GGGTCTTTAT TACATTATTG

CATCTGTGTC AATAACTCTG GTCTTTCTGT TAAGTTCCAG TCTCCCATTT TCAAATGTCC

CCAGACATTT CCAATTGAGT ATCTCTCCAA TGTATTTAAC CTGCTAAATA TCTAACACAT

AATCTTTCCC ATCAAATCGT TTCCTCTTAA GCTTTTCGTT ATTTCCTATT AGACTCCTGC

ACTTCTCCCA GGAGCCCAGA CTTAAAACCT TGAATTTCTC ACCATAACCT CTCTTTTGTC

TCCCATAATC AATTAGTAGC AAGTGTTATC AATGATTACT TGACAATATC TTTTTCTATT

TCCCTCCCTG CTATGATCAT TCATCTAGCA AGAAGAGTTG GCCCTTTGTA TCTGTGGTTT

FIGURE 6 (42)

CTGCATCCCT GGATTCAACC AACTGTAGAT GGAAAATATT TGAAGAAAAA AGCGTCTATA

CTGAGTATGA AAAAATTTTA TTTCTTGTCA TTATTCCCTA AACAATACAG TATAACAACT

ACAGCATTTA CACTGTAGCG TATAGATCTT ATAATCTAGA AATGATTTCA AGTACACCAT

TATATATAAG GGACTTGAGC ATCTGTGAAG TTTGGTATTT GTGGGGCATA CTGGGACCAA

TTCCCCCATG GATACAGAGG GACAACTATA TTTACTCAGT GCTTACTAAA TACCAGTTGG

CCAATGTGTT TTTCTTTTTC TGTTTTCCTG TCTTTAGTTT GCCCCTTGCC AATTAATTCA

ATAGTGCTGC CAATGCCAGG TGTACCTTCA GAATATTCTA TTCTAATTTT GTCATCTCCA

AGCTTAAAAA TATTTAATGG GCCAGGCGCA GTGGCTCACA CTTGTAATCC CAGCATTTTG

GGAGGCCAAG GGGGGGTGTA TCACTTGAGG TCAGGAGTTC CAGACCAGCC TGGCCAACAT

GGCGAAACCC TGTCTCTACA AAAAAGTATA AAAGTTAACC AGGTGCTGGA GCATTTGCCT

GTGGTCCCAG CTACTCAGGA GGCTGAGGCA GGAAAATCAC TTTAATCTGG GAGGTGGAGT

FIGURE 6 (43)

TTGCAGTGAG CCAAGATCTC TCCACTGCAC TCCAGCCTGG GTGACACAGC AAGACTCTAT

CTCAAAACAA CAATAACAAC AACAACGAAA AACATTTAAT GGCTGCACCT TGCCTGTGAA

AAATGCATTT CTTGGCCAGA TGTGGTGGCT CAAACCTGTA ATCCCAACAC TTTGGGAAGC

TAAGGCCAGG AGTTCGAGAC GAGCTGGGAT ATATAGGAAG ACACAATCTC TACAAAAAAA

AATCCACAAA ATTAGTCAGG CTTATTGTTC ATGCCTGTAG TCCCAGGTAC TCAGGAGGCT

GAGGCAGGAT TCCTCAAGCC CAGGAGTTCA AGGCTTCCGT GAGCTATGAT GGCACAACTG

CACTCCATCT TGGGTGACAG AGCAAGGTCC TATCTCTGGA GAAAAAAAAA AAAAGAAGGC

ATTTCTTAGG AGAGTTCTTC TCTGTAGAGT CCTAAGGGTT CCATGGAACT CCTTAAAAGC

ATCAGAGTAT GTGAGTGCAA TGGGAGGAAG CATTTAGCCA GAGCAGTTGT GCTCCCATTG

CATATTAATT TTTAAAAAAC AAAGCTATAA AAAAAAGTTG AAAACTACTA CGTTAGCATC

AGCCTGACAT TTAATGGCCT CGTAAATCAA ACCTTAATTG ACTTTTTAGC CAGTTATGCT

FIGURE 6 (44)

ACTAGCCAAC TACAGACAAC ACACTTTTTA ACCAAATTAG ACTAATAGTT GTCATCAGTG

GAAATCAAGT TTGCCATTCT TCCATGCCTT TGCTCACACC ATTACCTTTT CTGGAATGTC

CTGTACTCAT CTTCCTGTGT TGAACTCTAT ACCCAACTTT AAAAACCTAG CTCAAAGTTC

AACACTTCCA TTCCATTTCA AAAAGAGCTT TCCTCTTCCT TAAAGTTTAA GAACTCATTT

TCATGAATCT TTTTGGCATT TATTGCACAC ATGCTTGCTT TGTGTTATTT GTGTTCAGCC

TCATATGCCC CCAAGGTGTT TTAGACTCCT TAACGGCAAA AATGATGCTC TAAACACCTT

TCTATCTTTC ATAGTGTCTT AGTCTGTTTG TGTTGCTATA AAGGAATACC TGAGGCTGGG

GAATTTATTT AAAAAAGAGG TTTATTTGGC TCACAGTTCT GCAGCTATAT AAGAAGCATA

GTGTCAGCAT CTGCTTCAGG TGAGGGCTTC AGGAAGTTTC CACCCATGGT AGAAGGCAAA

GGGGAGCAGG CATCACATAT CAAGAGAGGA GGAAAAAAAG GAAGGAAGAA AGGAGGGTGC

CATTCTCTTT CAACAATCAG TTCTTGTGGG AACTAATGGG ACAAGAGGCT GGGCACGGTG

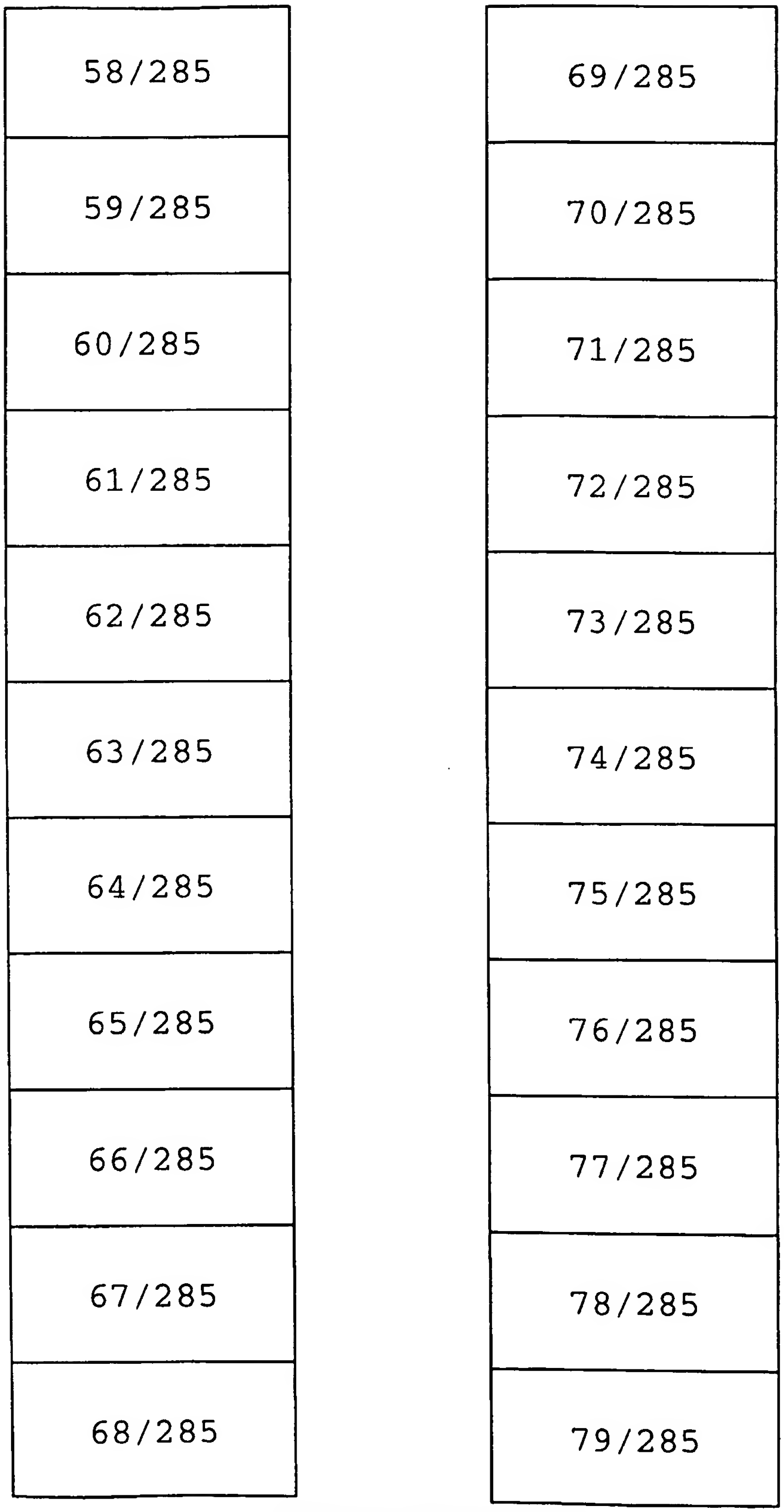
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FIGURE 6 (45)

GCTCATGCCT GTAATCCCAG CCCTTTGGGA GACCAAGGTG GGTGGATCAC CTGAAGTCAG

AAGCCTGAGA CCAGCCTGGC CAATGTGGTG AAACTCCGTC TCTACTAAAA ATACAAAAAT

TAGCTGGGCC TGGTGGCGTG TACCTGTAGT CCCAGATACT CAGGAGGCTG AGGTAGGATA

ATCACTTGAA CCCGGAAGAC AGAGGTTGCA GTGAGCTTGT GCCACTGCAC TCCAGCCGGG

GCAACAGAGT GAGACGGTCT CAAAAAATTT TAAAAACTTT AAAAATAATA GAGCAAGAAA

GCACCAAGTT ATTCAGGAGG GATCCACCCC CAATGACTCA AATACCTCCC ACCAGGCCTC

ACTTCCAACA CTGGGGATCA ATTTCCGTAT GAGATTTGGA GGAGACAAAT ATCCAAACTA

TATCACATAG TAATGAACAT AGTACCTTAT CTATAGAAAG CAATGGCTAG ACAACTGTTG

AATGGCTAAC CAAATCTGCT TTCCTATGGT CTCGCTCTAG AGGGGGTCAG TATGAGTTTC

TGTCAAAAGG AGAAAAAAAA ATGTATAGTC AGTTTTGTGT GTGTGTGTGT TCATGTAAAA

GAGATCAAGA GAAAAGAACA AGAGAAATCA TGAAAAGGAG GGGGAATATA AGAATAATAC

FIGURE 6 (46)

ATAGAAAAAA GCAAATTATC TTGTTTATCA GTAATACCCA AGGGGGTAGA AATGGTAAGT

AATAATCCTT CTTCACTTTG TCTGTAGTTC ACTTTTTTGC ACCTTTATTT TGATGAATTC

ACATCGAAGA CATTAACTCA TTAAGGCTTC CAATATTTTT GGAGATAAGA AGGGCTGCTA

TGCTCTTTAT AGATGGAAAA CTTGGGTCAT TAATAACTCA AACAAGGACA TAACAAAGAA

ATGGAGCATA AACTGCCAGG TCCTGACTGT AGATTTGGAT TCCCAGTTGG TGTCTTGTCA

CCCTTTGTTA CTCTTCCTAA AGTTATGATC TTTTCTTGTG CATAGGAAAT TCATAGTGAT

TTCCCATCAC CCTTGGGATT ATCATAGCTC CTTTAAGGTC CCCTCTATGC ACTCAATAAC

ATCAACAGTA AGTGTTCTTC GAGCACTTAC TGAGTGTATA TCATTGTGTT CTCACGCAGC

ACCCACAGAT CTCACCAAGA ACCTAGCTGA AGCCTGTAGA ATGAATAGGT AAGTACTGCC

ATGCCAATCT GGAGTACTCA AGCGATGCAA ATGATTCCTT TAATTGTACT TTTGCAGGCT

TGTCAGTTTT GCTCATGGAG AAGTGGCTAC TGCATCCATG TTATATCTAT GTAATGTTGG

FIGURE 6 (47)

ACTGCGAAGC ATCACTTGAC TTTTTCCAAG CAGAAATTAC AGCTGATGAC AAGCTGCTGC

TGAGAAAATG GATATTTTTC TGAATTCAGT TCTACGTGGA AACAGCTGAC TAGTTTCCAT

TGCTGTAAGA ATGGCTCTTT TGCTCTTGGT TGATTTTGAG TAATGGCTTT ACTTCTGTAG

AAAGGAGATT TCATTTGAAG TCCACTCAGG GATTTGGTTC AACAAACTGG AGTACAGGTT

TCAGAAAATA TCTCTTTAAT CCTCCAATAA TAAATTTTCT CATCTATAAT TCCTGGAACA

CTTCATCCTT TGCAGCCGAG CATATAGATA GATTTGTTGC TCACTGTGTT CTGATTGCCA

CTTTGACCTG CTTTTTCAAC TTAGGTTACA AATAGAACAG AATCTCTCTG ATTTTTCTCA

TTAATTGTTT GAATTCCCAC TTTTCCTCAT TAGCAAGAAG TCCAGTATCT TCCTGAGAAC

TTCCTTTTCT CAATCTAGGA ACTTACTTGG TCCATAAGGT AACAGTCTTA TTTCTGACTA

TCAAGGAGAG AAATAACAGG AGCCATTATC ATCTTCATGG TGTCACTTTT GAAAACTGGT

CCTCTGTAGA TCTTCAGATT CTTGCGTTAG TCCATTCAGC TGCTATAACA AAATTGCATA

FIGURE 6 (48)

GACAGCATGG CTTATAAATA ACAGAAATGT ATTTCTGACA GTTCTGAAGG CTAGAAAGTC

AAAGATTAAG ACACTGGCTG ATTTGGTGTC TGGCGAAGGC CCATTTGCTC ATAGATGGAC

GATGACCTTT CACTCTGTCT GCACATGGCA GAAGGGCAAG AGAGCTCTCT GGGTCTTTTT

TATAAGGGCA CTAATCTCAT TTTTGAGGAC CCTGCCCCCA TGACTTAATC ACCTCCCAAA

GGCACTGTCT CCCAATACCA TCACCTTGAG GGTTAGGATT TCAACATATG ATTTTGGGGG

GACAGAAACA CGCAGTCCAT CTCGCTTGTC CACTCCATGG TGGTATTCTT GCTGGATCAG

TTTCCTCCTT GGGGTGCATT TGTGTTCCAT GTCTAACTTG CAAGTTATAG CAGGCCCGAT

AGCAAAGTAT TCCAATGTTG GTATGCAGAG GCATTGAATA ATCAGAATGA ACCCACGCCA

TAAACAACTG GTAGAGCTGC AGAGAGTACC AGCTGATTAT GAGCCCTGGG TAACAGTGGT

TTTTAGTTCC TATGTCCGTC AGCCCTTTTC TCCCATAGTA GCCCCACTGT GTTGAAGTGG

CTGAATCGAC AGAAGCTTCC AGCTTGGGCC ACATGCTCAT GGAACCAATT CTCCTTATGA

FIGURE 6 (49)

GCCGTACAAG AGCTGGGTTG CCATTCTGGA TACCCTCTTT TTTCAAGAGA TTTTATTTCA

AGGATATTTT TTCTTTTATC AACTACAGGG ATTATTTAGA ATCTTAGGGC AGTGGTGCCC

AACCTTTTTG GCCCCAGGGA CAGGTTTTGT GGGAGACAGT TTTTCCATGG ACCAGTGTCA

GGGGGCTGGG AGGCATGGTT TTGGGATGAG TCAAGTACAT TACGTTTGTT GTATACTTTA

TTTCTATTAT TATTATATTG TAATATATAA TGAAATAATT ACACAACTCA CCATAATGTA

GGAATCAGTG GGGAGCCCTA AGTTTGTTTT CCTGCAACTA GACAGTCCCA TCTGGGGGCA

ATGGGAGATA GTGACAGATC ATCAAGCATT AGATTCTCAT AAGGAGTGCT CAGCCTAGAT

CCCCGGCATG TGCAGTTCAC AATAGGATTT GCTCACCTAT GAGAATCTAA TGCCACTGCT

GATCTGACAG GAGGTGGAGC TCGGGCAGTA ATGCGAGGGT TGGGGAGCAG CTGTCAATAT

AGATGAAGCT TTGCTCGCTC GCCTGCCACT CACCTCCTGC TGTGTGGTCC ACTTCCTAAC

AGGTCACAGA CTGGTACTGG TCCATGGCCA GGGAGTTGGG GACCCTGTCT TAGGGAGTAG

FIGURE 6 (50)

GGGTGGAGTT CCCTTCACTT CTAGAAGGCC CTGGATTAGT ATCCCAGAGC TGTCATTACA

GAGTATCACA AACCAGGTGG CTAAAAACAG ACATGAATTC TCTCTTATTT TTGATGGCTT

GGAAGTCCAA AGTCAAGGTG CTGCCAGGGC CATGCTCCCT CTGAAATGTG TAGGGGAGAA

TCCTTCCTTC CTCTTTCTAG CTTCTGGTGG TTTGCTGGCA ATCACTGGCA TCGCTTGGCT

TGCAGCACTT CAACATCTGC CTTTACTGTC TCATAGTGTT CTCCCCTCAT GTCTCCAGGT

CTCTCTGTCT CTCTTCTTTG TATAAGGAAA CTAGTCATAT TGGATTAAGG GCCAACCCTA

CTCTAGTATG ACCTCATCTT AAGGTCACAT GCAATGACTA TTCCAGATAA GGTCACATTC

TGAAGAACTG GGAGTTAGGA CTTCATATCT TTTGAAGGAA CACAGTTCAA CCAATAACAG

CCCCTGTACT GTTTTACAAA TAGGTATTCC TCTCCTTCCC AAAGTTCTTC ATAGCAGAGA

CAACTTGTAC CAAAAGGCAA AATACCTTAT TATGTAACCT TAACCTAGGA TCATAGATCC

CTACTGTCTG GTGCTTTATA AGCACAGAAC CACCGGGAAA TCATTATTAA GACAAGGAAA

FIGURE 6 (51)

GGCCAAGTGC AGTGGCTCAT GCCTGTAATC CCAGCACTTT GGGAAATTGA GGCGAGTGGA

TCAACCTGAA GTCAAGAGTT TGAGACCAAA CTGACCAGCA TGACAGAACC CCATCTCTAC

TAAAAATACA AAAATTAGTT GGGCATGGTG GCATGTGCCT GTAATCCCAG CTACTCAAAA

GACTGAGGCA GGAAAATCAC TTGAACCGAG GATGCCAAGA TAGCAGTGAG CCAATATCGT

GCCACTGCAC TCCAGTCTGG ATGATAGAGC AAGATCCTGT CTCAAAAAAT TAATAAATAA

ATAAAAAGAC AAGGAAAGCC TTTTCCAAGG AGACCCTTCT GCTTTGCTAG TTCAGAGAAC

TTCTCTTTTG GAGAAAACAA ACACCCAGTC CATTAGCAGC AACGTCAGGG ATTGAATTCT

TAGGGCAGCA GGCTGGGCAC AGTGGCTCAT GCCTGTAATC CCAGTACTTT GGGAGGCTGA

GATGGGTGGA TCACTTGACA TCAGGTGTTC GAGACCAGCC TGGCCAACAT GGTGAAAACT

CATCTCTACA AAAAATATGA AAAAAAAAAA AAAAAAAAAA GCTGGGTGTG TTGGCTTATG

CCTGTAGTCT CAGCTACCTG GGAGGCTGAA GCAGGAGAAT CACTTGAACC CGGGAGTTGG

FIGURE 6 (52)

AGGTTGCAGT GAGCTGAGAT TGCCCTACTG TACTCCAACC TGGGTGACAG AGAGAGACTC

CATCTCAAAA AAATAAAGAA TTCTTCGGGC AGCAGTCTTT CCTCCACCTC ATAGACCATG

GAGGTGAGCC AGCTCTGACA AACCATGAGA ACAATGGCAG AGACATACCT GTAACGTAAC

TGACTGGGGC AAAGACAAAG GTGAGGAAAA TGACAAGTTT GAGGAACTAT GAGACCAGGC

AGTGGGGAAC ACCACTAGCA GAAATGATGG AAGTTCTCAA GAATAACAAC AGAGAAATAG

ACCATGGCCA GAGTCTAGAA CCCTCCAGGG AAAGGAGATG GGCTCCAGAG GCAGAAGAGG

ACGTTGAAGG GAATGGGGAG TGGGTGAAAT ATATAGACGA TGGGGACCAC CCAAGAGCAG

TCGCTATTGC AAAACTGAGG AGAAGGAGAG TCTGGAGGGG GTGGTGGGAA GCTGGGTCTC

CTAAGGAGGT TTTGACAAAA GCAGTCATGG AGCGGGCTTA GAAATCACAG TTGGGGACAG

GGTAAAGTTC CTCGGGATAT AGAGGATGAG ATTAGAAGAG GTTCCAACTA GGGTAGTGTG

GAGAAAAGCA CTATTGACCC AAAAAGGAAG GAGAATGTGG GTGGAAGTGG CAGAGAAAGA

FIGURE 6 (53)

GGGGTTTGAG CAGAGAGTGG TGATTTTTCT AATGCAGAGT TGTGGGAGGT GGAGTGCAGG

GAGCCAGGCT GGGTGGCTGT GCTGATGTGA TTAAGCACTT ACTGACTGCC AGGCAATGGG

CTAAGTACCT GAGATGCTTT GTCTGTTATC CCTCCCGAAA CCCCTCTGAG CAGGTGCAGT

TATTATTCTC ACTTCACAGA TAAGGAAATT GAGGCACAGA GAATTGAGTA ACTTACCCAA

GGTGACATAG CTCATATATG GTAAAGCAGG CTTTGAACTC AGTCTAGCTC CCGAACCTAA

GCTTGTAACT ACTATGCTTT TCCCAAAAAA AGGGGGCTGG CACAAAAAGA GCTGAGGGGG

CTGGGCATGG TGGCTCATGC CTGTAATCCC AGCACTTCGG GAGACTGAGG CAGGTGGTTC

ACCAGAGTTC AGGAGTTCGA GACCAGCCTG GTCAACATGG TGAAGCCCTG TCTCTACTAA

AAATACAAAA ATTAGCTGGG TGTGGTGGTG TGCACCTGTA GTCCCAGCTA CTTTGGGAGG

CTGAGGCAGG AGAATCGCTT GAACCCCAGA GGCGGATGTT GTAGTGAGCC AAGATCATGC

CACTGGACTC CAGCCTGGGT GACAGAGTGA GACTCCATCC AAAAAAAAGA AGAGCTGAGG

FIGURE 6 (54)

TGATGGCCAC CATCAGCATC AGCCTGGAAG TTATAGCAGG ATGCTAAGTT TCTCTAAAGC

TGTCTTTCTT AGGACTTGAA AAAGATAACT TGGGTTTGTA TCCCATCTCT GCCATTAGTA

GTTTACTGGC TTTGGATAAA TTACTTAGCC TTACTGAACC AACTTTGGAT TTTTATAGAG

ATACTGTAAT GAAAGGAATA AGGTATCAGT CTTAGCAGAG CATCCAGAGT GTTCCTATTA

AAACCTAAAT CATATCCTGT CATTGCTGTG CCCCAAACCA TTCAATGGCT TCCCAACTCA

AAGTTAAAAA CTCATCTTTC CAGTGGCCTG CAAGAGCCTA TGCTATCCGG TGTCTGACCT

CATCTGTTGT TCCTTTCTCC CTCCCTTTCT TGGCTCCAGA CGCACTCTGG TCTCCTTGCT

GTTCCTTGAA TACACCAGGC ACACTCTCTT CGCCTGAAAC ACTTTACCCC AGATATCTTA

GCTTACTCTC TGCCTCCCTC AATTCATTGA TGAAATGTCT CAGTGAAGTC TTCTCTCTCT

CCTCTGTAAA AGTATACTCT CTGTTCCCCT TCTTTACTGT TCTAGCTACT ATTGCTGTGT

AACAAATCAC TCCCCAAATT TAATGAGTGA AAACATCAGC CATCATCTTA TTTCTCACGG

FIGURE 6 (55)

TTTCTGAGGG TCAGGAATTC TGGAAGGGCT CAGCTGGGAG GTTCTGGCTC TATAATCTCT

TATGCAGTGA GAGTCAGATG CTGGCTAAAA CTGAAACAAA GCAGGGTTCT AGTAGCTGAG

GGCTGGCTGG GTCTCTCAGA TATAGTTCAG ATCTCCTCCA GGGGGTCTCT CCACGTGGGC

TAGTCTGAAC TTCCTCACAG CATGGTGGCC TCAGGGCAGT GGACTCTGCA TAGTGGCTGA

AGGCTTCGCA GCTGAGTATT CCAGCAAGCA AAGTGGGAGC TGTATTGCCT CATATGACCC

AACCTTGGAA TCCACACAGC ATCACTTCCG TGTATTCTAC GGGTTGAAAA GTCACAAAAA

CCAACCAGTT TCAAGGAGAA GGAACAGAGA TCACATTTCT CAATTGGAGA AGGGTCAAAG

TCACATTGTA ATCAGAGCCT ATGGGATACG AAGTATTGCG GTCAGGTATG AAAAATTTGA

TTTGCTGCAT CTGCTTTACT TTCTCCACAG CGTTCATGAT CTGCTTCTCA CATGATATTG

ACTTACGTCA TTTCTGCGTT TCCTGTCTTC CACACTAAAA TGTCAGCCTG TTTTGTTCAC

TGCTGTATCC CCAGAGCCTA GCACGGAGCC CAGCATGTAG TGGTATCCAA TAAATACTTG

FIGURE 6 (56)

TTGCATGAAT GAATTCTGTC TTTTAATCCT AGCTATAGGT TTCTAAGTTA AATATTACTA

TAATCATCTT ACAGACGAGG GAAATGAGGC TCAAGAAGAT TTGGTAACTT ATGCGGGATC

ACTCAGCCAC ATAATGGAAG AGACAGCATT GAAGTACACA TGCTTGCTCT GTCTGCTCTT

CCAAGCTGCT CATCACACAG CTGCACCTCT GAGGACTTCC CTCCCCAGTC CACCTCCACC

CTTACCCAGA GACACACATG GCCACAATCC ACTAGCAGAC CAAAATTCAA TTTTTCCCCA

GTTGGTTGCA CTCAAGCTGA GAGCAAAGCA ATTGCACTTT AAATCCCCTT ACAGCAGATA

TTTCAGAGCA TGTTCGGAAG AACCCATCAC ACTTGGCTTT TAGATCTTAT TTCTGGTTTG

TTACAAAAAC ACAATTAAAT GAAAGGTTAG GTAGCTTTTG AATGGCCAGC TCAAAGTTTT

GGCTTATTTT TGCCTTGCTG TCTTTATAGG CATTTTACCA ATATTTATCA CTATTTCCCT

TAGGGAACCC TTAGATCTGT GATATTTGAA ATAATAAAGC CTCTCCATTG GCCCTTTAAA

AGGTTTGTGG TAAAACCACA CCATTAACAT TCACAGTTCC TTATTTATGA GGCCTGATTG

FIGURE 6 (57)

CACTTATTTC CATATTTCTC ACTGTTTCTC CGATGAGGAT TTCACATAAT AGTGTTTGAA

GGCTAAAGAC TTCAAAGCAG ATTCTTTACT ATTTTTATCT TGAAAAATAT TCAATATTTG

TGTAATTAAA GTGAAGTCTT CCTAGAGAAA ATGACAACTC AAATAATCTT AAATGTACCT

CCAAGAAAAA AGCTGTCAAA GTGACATTTA GTAATAGAGT CACATTCTCT AAGGCCTTTG

CTTCTCCTTC TGATTCTTAT CATCTTTGAA GGTTATGTCA TGGGCTGACT TCAAATCAAC

TTTTAAAATT ATTATGGCCT TCTTTAAATG TGAGTTCTGA AGGTGAGGGG CTTTATCTTT

CTTTTGCTCC AGATTTTTTT TACCGCGTCA TTACCAAGCA TCTTAAAACA AAACCTAAAA

ACAAAAATCT TCCTTGACCT GGTTTTTCCC ACTAGCTAAC ATCCTATTTT TATCTTTCCC

CTTTGCACTA AAGGTTTTTA AACGGATCTT TATACCCTCT GTCTCCATTT TCTCATCTGC

TAACTTATAT GGCAAAGATT ACCACTGCCT TTCAACATAA TTGGCCAATC TACAGAAAGT

TTTCAAGTTC TCTTTTTAAT TGACCACCTC CTGCCTACCT CCCCACCTTT GACATCTTGC

FIGURE 6 (58)

TTCTCACTTG GCACCTTACC CAGTGTTCAA GATTCCCTCC TTTAGGATGT CTTCAGAGCA

GCTACACAGT TGGTACTATA ATTTATACAT CCTTGTACAC AGGGCTTGCT GGGATATTGA

TGGAGAGAAG GAGGAAACTG GAAGTAGTTC AGGCCAGAGC TAGGGAAATT GACCCATCTC

CAGGTCTCAG GTCTGCAAGG GGAGCTCACA GCTTAACACA TGGAGTCTAG AAACTTGTGC

TGGACCTTGA CCAACACCAG CCCATGGAGT CCAATACAGT GCTCAATAGG GATTTCCAGG

AAATTGCTAT ATTTATTCAA AGAGAACTTA CCAAGTGTCA GCTACGTGTT GGGCATTGTG

CTAGGCACAG GGACCACAAA GATAAGACAT TGTAGCTTTC CTTAAGTTGC TCACTGAGTA

AATAGAGAGA CAGAAAGGTA AACAGGTAAG TGCAAAAATA CATACAATTC AGCAATAGTG

TTCATAGTGG CTATGGAGAG AACGCTCACT AACTTTGTTT AAACAGTTGT TCTTTCAAGG

ATTTGACATG GATTTGATTG GAAAAGCATG ATACCATTTT TTGCAATTAA ACACAGGAAT

ACATAAATAA AATGCATCAG TATTTTTTAC AAATAGCTAC TAAGAGCTAC TAGAAAACCT

FIGURE 6 (59)

GGGAATTCTT AAAACCTTAC CATGCTACTT GCTCTAAAAT ATTTTATTTT ATGTTATTTT

GTACATTTCT TTACCTACAC AAACACCACT GTTTTCTTCA TTTCTTAGTC TATTTAAACC

TCACACCCTT TCAGCATCTC TTAATTATTT ACTACCATCT GTTAGTTCTC CTGTCCTGAA

TGAAACAAAA ATGGCAGAAT GTAAAACGAG GGCGAACAGA TTTTTGACAG GAAGTATTCA

GAGGTAGAAG GAAATAGTCA AGACACATAT GATAAACGAA AACAATAATA ACTTTATACA

TAACAACTTA TAGACACATT TAAAAAGTTT AAGATCTCAA GAGCTATGTC TGAATAGATA

GGAGTAAAAA CTCTATTAAG TAATTAGGAA AATAACAAGA ACAGTGAATT TCTTAATGAA

TGGCATGTAA TCAAAACTGT ACTTATCGTC TAATTCATAA TCTTGAATGT TTTTATTTTA

TTTATTTATT TTTTTATTTT TTGAGACAGA GTCTTGCTCT GTCACCCAGG CTAGAGTACA

GTGGCGTGAT CTCAGCTCAC TGCAACCTCC ACCTCCCAGG TTCAAGCGAT TCTGCTGCCT

CAGCCTCCTG AGTAGCTGGG ATTACAGAGG CCTGCCACTG CACCCGGCTA ATTTCTGTAT

FIGURE 6 (60)

TTTTAGTAGA GATGGGGTTT CACCATCTTG GCCAGGCTGG TCTTGAACTC CTGACCTCAT

GATCCACCAG CCTTGGCCTC CCAAAGTGCT GGGATTACAG GCGTGAGCCA CCACGCCTGG

TCGAATGTCT TTATTATTTG AAGAGACAAC ATGGGCCTTA AATCTGTCTT CTATTTGACA

GACTTTGATG GAGTCAAATC CCAATGCTGC CACTTACTGA ACGGCCTTAA ATGACTTAGT

CTCTCTCAGC TGTCTTTCTG CATATGTAAG GTGGAATAAT GATGGCTTTC AAGGAGGAAT

AAACCTATGA AAAGTGTTGA GGATAGTGTT TGATATGAAA TAAGGATTTC AACAAGTAGT

AGCTGCTATT GAAGATTTAA GAGTTATTTA TTACAACTAT TTAATAAAAT TTTAAAAACT

AATACACTTA AATTATTAAA GAGCTTTGAA ATGGGCCAGG CGCAGTAGCT CCTGCCTGTA

ATCCCAACAC TTTGGGAGGC CAAGGTGGGC GGATCACCTG AGGTCAGGAG TTTAAGACCA

GCCTGGCCAA CATGGTGAAA CCCTGTCTCT ACTAAAAACG CAAAAATTAG CCAGGTGTGG

TGGCATGCAC CTGTAGTCCC AACTACTCAG GAGGTTGAGG GAGGAGAATT GCTTGAACCT

FIGURE 6 (61)

AGGAGGTGGA GGTTGCAGTA ACCCGAGATG TCACTGCACT CCAGCCTGGC AACAGAGCAA

GACTCCATAA AGACAACAAA AGCTTTGAAA TTGTGTAAAT GAGTTGTACC TATCTTCATT

TAAGAAATTC ATCTTTGTTC ATTTATTTTT ACTTGACATG AGAGCTTCCA GCAATTTTTA

ATTAAGCCCT CACAGATTTT ATGTCACTGG CTATGTGATA AACAAATTAT TTGCTAAAAT

AATATTCTTG CTTCTTTTTT AAGGAATTGT CTCCCTAGAA ACGGTTTGTA CCAAACAATA

CACTGACTTT ACACAAAATC AGATCTGATT GGCAACAGTT GCAGATGTTT TCAAAAGATT

TTCATTTGAG AAGGGGCCCA TTTGGGTTAT TTAGATTCTA AGAACTGAAA CTGCTTTGTT

CTGTTTTTCT GGCTTCTGGG AGAGGAGGAG ACATGAATTC AGTTAGCACC TTGGTATTTT

CTTTATCCTT CATTTCAATA CAGAAGATGC TTCATATGCA CAGTGGTGTC AGGTCACATC

AAAAGAAAGA GAAACAGTTT CTTGGTTTTT AATTTTCAAC CGGAAAGGAA AGGCACCCAT

TTTGTTCCGC TCTAATTAGC CAGTGCATGA CTTAGAGAGC AGGCAGATGC TTTGAAGGCG

FIGURE 6 (62)

TGGTAACACA GGTCTTCATT AATCTCCACG CAGGACTTGC ACTTCTACTA TGCCTAGGCT

GAAGAAAATG GCTCAGGAAG ATGAACAATC TCACAGAGCC CTAACTAACT GAAGCCAGGT

GTTATAAAGC ACAAGTCAAG AGGGTGAGAA ACTAACGTTC TTGAAATCTC CCACTTCTTT

CTACGTCAGA AGAGCCAAGC TGATTATTTT AGTTGGAATT TAGAAATTTT TAAAAATTAT

TCTAAAGTCA TGAACAAGCC TAATTATAAA GATAGTTGCT GTGAAGGTGC TGAAATAACT

CGATTTTACC AACCCCCTCT TCTGGAGGAA GCCATAATGG AATCCTGTAC AATGTTCACT

CTACCAACGA ACTCTTGTTT TTCTAATGAG GAAACAGAGG CCCACAGTAT TAAACTATCT

TAACCAATAC AAAATGACTA GTGCTCTGGT CCTTTTATTA AGCACTAAAA TTTTGATCCA

ATAATAAATC TGTCCATTAG AAGGAGTTTC CCTAATGTAC TGGTTCTAAC TTGTTCCCTT

CAAGGGGCCA GTGTCCCGTA CACATAGCTA AATGGACTT CTCTTCAACT ACCATTACCC

AGAGGGCAGA ACCTAAAATG CTGTGAATGA CATTCTGCTG TTCACATCTC AGCAGCA

FIGURE 6 (63)

GTGTTGCATT TGAGCTTCTG CAGGGCCACC CAGGACCTAT ATCTGCTCAG ATGTTTAACT
CATCTAATTC AGTGAACACT TCATTCTAGT TAACTGAACA TCTACTTTGT ACAAGGCACT
ACAGCGGTTC AGAGATGAAT AAAATCATGA GATTCCACTG TCTCCTATAA ACCATCACTT
TGGGAAATTT TAGAAATGTG GGTAAGCTCC AGGGCTTCCT GCAGCGTAGA AGTCACAAAC
TCAAATGCCT GCAGAGGCCC AGCTGACAAC ATAAGTAAAT GATTCTGGCT GGGCGGAAAA
CAATTACGGG TGGGTGGGTT TCCAGCTGGG GAGTGCACGC CTGTGTTAAA GGACAGCTGC
TACTCATTTC CAGCCAACTG TGTTCCCATG TAGAACTGCG GCCCAGTGTA GCCAGTACCG
AAGATTTCTC AGAAAAAGCC GGAGATCTCA ATGTTAGTGT AAAATCTCTC AAATTTCCAA
GAGGATTATA TGGGGCAAAG GTTCTCAGAT CAGTTTGCAG TCTCTTACTT AGCCCATGTG
CAGAGCAGTC GTAGAGGGTA GCATGCAGTG TCCTACATAA TAATTCTTTT TTATTTTATT
TTATGCCTTC CTCCTTCCTG TCTCTCTTTA ACCTTTCTTC TTCCCTCAGG CTGGCTTCTT

FIGURE 6 (64)

CCCTCAGCCT CGTCCGACCC CAGCCTGGGT TCAATGAACA TTCGGTAAAG GAACACGGAA

TGTCAAGCGC ATTAGAGACA ACCTTGAGAC ACATTCCTCT TGCGGTAAGC ACTTCACTGT

AGATTTTTAA TTTTAAACAA GACAATGTTT ACGACTTGCT TCTTTCAGGG AAGAGCGATA

TCAATTTTAG TGAACACTTC AAGGCTGAGA TACGCTAGGA GAGTCGTGTG GTGTTGCACA

GCAAAGAATT CCACTTTGAA GCGAGTGGGA AAAAAAGCAT CAAATGCCAC ATGTAACTCA

CCGCCTGAAG GGTTACATTG GTATGAAACC TGGGTTTAAA AAGGGACCGA ATAGACTAGC

CATTAAAAGA CCTGCGTACA ACCTCTCTCT CTCTCTTTGA GAGATAATGT ATCTGGACAA

TAAACATGAA CAGAGTGGAG TCTATCCTGT TTAAAACATT GCCTACTGTA CAGGCACCAG

GAGCTGAAGG GTCAGAATAT TAGCAGTGGG AGCTTGATTA GAGTTGATGA GAGATGGGTA

GTAGGAGGAA AGAGTGAGAT AGAGGAAGAG GACATGGGGG TTACCCATAA GTGGAGAGTA

GAAAAGTAGA ATCAGCTGGC CATCAAAGGG CGTGGGACTG AGGAACAGTA TGGCATGTAT

FIGURE 6 (65)

TAAATATACT AAGCGCTGAC ATTGGAGGAG AACTAGGAAG TTAAATGAAA TCAATAGGGG

ATGATGGAGA ATAGTTAGGT GTGCAGGGAT TAGGGTTATG ATAGAAATAC ATGTGAATAC

ATGCAGTATT GTCCTGGAAA ATGGTTAACA GTTGGTTCTC CTGGGGGGTG AGGGGAAGCC

CTGATTTGTA ATATTTGCCT ATTTCTGTGG TGCAAATACT CCCACCATGA CCAGTTTCAA

GCTATGAATG TTGAAGTCAC AGAAAGCAGG TTGGGAGGAG ATGCGCACAT TTGTTCCCCG

GCAAGGTGGA AGGTAAGGAA GGTGAAATCA ACAAGGTCAA AGAAAACTCA AGATTTCGAG

GTGCCTCAGG TCTGAGGGGC AATGAAGTCT AGGAATGGCT GTGCTGAGGT AGCTGAAATA

GAAGTGACTG CAGAGGTCAT GAAGCTGAAG AGGTGAAAAC AGAAATTAGA AAGGCAAACC

CCCACCGCCC AACCCCCACC CCTGCAGCCA GTTTCTGAGG GTGACAATAG AGGAAAGGGT

GGAGATGGAG TTCAGGTCCA GAAGCCATAG AAGCGAGTGT GACATTGTGC TCAAGGTCAG

CACATGTCAG TGTGGGGTGT CACATGCTGT TGTGAACCAT CATTTATCAC CAATTATGGA

FIGURE 6 (66)

AGACCTCCTA TGGGCATCTT GCCATATGCA TTATAAAGAT GTGTAAGAAG ACATTTCCCT

CCACTTGGTG AGGAGAATTA GGGCTGTACA CAGATACTGT AGAGTGCCAT GTGCCTGGTA

CAGATAAGGT GTGTTAGAGG TTAAAAGATG AGGCTCTTAA TATTAATGAT AGATCCCACT

TACCTGAGTC TGACTTACAA TGTGCCTAGC ATTAAGTGTT TTACCTGCAT TCCCTTTGAC

GTTCAGAACA ACCCATTTTA CAGATAGGGA AATTGGGTCA GAAAGTTTCA GTAACTTATC

CAAGGTCAAC ACAATTGGCA AGTGCCAGAG CTGAGCCAGG AACTGAGGTC CTTCTAACAC

CAAACAGCTT GTCTCCCCAA TCACTGTGCT ATTTTCCTCC CCCAGAAGAT AATACTCTGA

TGGAAATGAA GGATAGTGTA ATAGGAGATT CGGTGTTCCT TTTTTTAAAA AAAATTCAGC

TTGCATATTC CTAAAGAGTC AATTCATGTT TAAAAAAAAT TTCCCTTGTG CTTGCATGTG

ACATGTATTT TTAGGATCTG CTGTTAGCAA GTGTATTTTT GTGTGATTGA GTGGGAGAGT

GGGAAAAGTT TTGCAGAGCT GTTGAAGCCA GAATGCAGGG GGGCTGCGCA GCAGAGACTG

81/285	92/285
82/285	93/285
83/285	94/285
84/285	95/285
85/285	96/285
86/285	97/285
87/285	98/285
88/285	99/285
89/285	100/285
90/285	101/285
91/285	102/285

FIGURE 6 (67)

TAAAATCTCT GCCATCTCAG GTCTTGGAAC AAGCACAAAG AGATGTGTTC TCGATTTATT

ATTCTATGTA CATCCCCAGA TGAATGACTA GTTAAAGGTA TTGTTAAAGC ATTTTAAATG

ACCCACTTCC AGCAGCGAAC AAAATCACTT GCTGTGCCAA GCCAACTGGC ATTTCTGAGA

TGATAAAACC ACAAAGTGAG GAAAACGTTA AAACTGCTAA AGCAAAAATG ATACACAATA

ATGGAGAAGG AGAAAAATTG AGCTTTATTG TCTGCCTAGG CAGATGGCTG ACCACTAGGT

GGGCCTCGGC GTCACGTCCA GGGTAATTGG TTGCTGGGGT GTTTCTGGCG AGGAAGATTC

ACGCTTCAGC TCGGTCCACA AGATCCTGGC TCATTCTTTC CTAGATTCCA TTTTCTGCCT

CCTCTCCATG ACTGGGTCTG ATGGTTGATC CAAACGGGCA ATTGAAATCA GAAGGTTACC

TTTACCTTAA AATGCTTTTC TGGAAATAAA AGGACATGAA AAGTAACTAA GGACCGGATT

TCCTAGCCGT CTTTCTCTCC TGCATGCGCA ATTTATCCCC AGATATAAAA TTGCCTGCTT

TGATAATTAT ACCCTCTAAA TGAGGGGCAA GTGGCTAATT ATGCCCACAT GTGGCCGATT

FIGURE 6 (68)

GCACTCCCCA TTAGCCAATT ATGTGCTCAA TTATTTGTGC ACATGAATAA TTGCACTCAT

GGAAAATAGC GCCCTCCTTT CAAATCCTCG TGCTTGGAGT GGCTGATGGA GTAATTGTCA

CACTGGAAAT GCACTTGGTG GGGAGGGAAA GAGTATCAGA TACCAGGAAA CGCATAAGTG

ACCAGAGCTC GCAGATGTTC ACTGCCACAA ATGGCCTTAG GAGCCAGAGA GAGCGGGAAG

GACCACAGGA TGGAACGGGC CAGCCTGTGA GTTAGGAAGC CTGCTTCTGA AGTTGCCTGG

GCAGCTCATG TGCGGTGACC TTGGGCAAGT CATTAACTTT CCTTCAGGTC TAACTGGTTC

TGCATACACA ATGAGGATGG TAATAACGCC CAATTCCCAT CACTATCGTG GGATGGATCA

GACTATTTAA AAGGATTTAC AATCTGCTTG GGTAAAAGCT TTACATAAAT ATGAGGCATT

ATCATGTCGC TTGGTACATC TCCAATTATG AAGGAAGGGT AATGACCCTC CACAGCAATG

CAGGACTCCT GGTTTGGAGG GAGGGAAAGT TTGAGAAGGA CAGGAAGCTT GTTGCCCCAG

CACTGATGTT TCTACTGAGG TACCAGAAAA TGTCATGTGG TCATACAGAA TTCATTTATT

FIGURE 6 (69)

CATTCAACAA ACATCTGTCA ATTGTTACAC TGTCCTGAGA ATTTGGAAAA ATGATGAAAG

ACTCAGTCCT GCCTTAGGAG GTCACTGGCA CATTGGCCCG GGCCCCTGTT TTGGGCCTTT

TACTCTGACC TGTGCTGATT TGCAAATAGT GGGAAATTTT ATCTCAAGTC TATGAAATCT

GGCATGCATT TTCACGGTTT GATTGCCAGG TACATTCGAT GGCAATGAGT CTTATAATGT

TTGGTTACCT TCATTTACCT AAGAACTGTG GTTGTTGCTG TGGTTGTTGT TTTTGTTGTT

TTTGAGACGG AGTCTTGCTC TGTCATCCAG GCTGGAGTGC AGTGGCATGA TCTCCGGTCA

CTGCAAACTC CACCTCCCAG GTTCAAGCGA TTCTCATGCC TCAGCCCCCT CAGTAGCTGG

ATTACAGGCG CGCACCACCA TGCCCGGCTA ATTTTTGTAT TTTTTGTTCG GGACACAGAT

TTCACATGTT GGCCAGGCTG GTCTCGAACT CCTGATCTCT GGTGATCCGC CTGCCTCGGC

CTCCCAAAGT GCTGTGATTA CAGGCGTGAG CCACTGTGCC CAGCCAGAAC TGTGGTTTTA

ATGACAATGC TAAAAAGTGG TATATGTCAC AGTGTCGGGT GGGGCTAAGA GGCACATTGC

FIGURE 6 (70)

TGCAGTGATC CATCATTCAT TTCCCACCAT TCTCGCCTGG ATTAGCGCAG CAGCTCCCAG

AGAGGCACCT CACTTTGACC TTCTTCCTCA AAGACATTCT CTGTGACCTG CCTGGCCCTT

ATTACCTCTC TAGCTTTGCC ACTTCCCTAT GTCTCCATCT CCCCTCTCAC ACGTAGTAGA

AAGAGACTCT ACCTCATGGA GTAAGGAGAG GCTTCACAGA GGCAGGATTG CTATTAGTCT

TCAAAGATGA GGTATTTGCT AAATGAATGA GACAAAGGGA TTGGGGCCAC ATTACAGGGA

AATTGAGGTA TGTAATAGCC TGGTGCAGGT TAAGAGTGTG GACTCTGAAA CCAGACTCAG

CCTGGAATTG AATCCTGGCT GTGTGATGTT GGGCCAGTGA CTTAACCTCT CTGTGCTTTT

ATTCACTCTT CTATAAAATG GGGATTATAA TAAACCTACC TTATAAGGTT ATTATAACAG

TCAGTAAATA TAAAAATAGA AGTTTTTGGA TGATGACTAT CACATCAGTA AACACTTGTT

TGCCATTATT TTTATTACTT GACTAAAAAT ATACCAAAAA GACCATCCAA GAAAACCCTT

TAAGCTGCTA GTGCAGAAAG ATTCCCCTTG TGTTTGTGTG CTGGGGGGTC AGTGGTGCCT

FIGURE 6 (71)

GTGGCCCACT GGAGAGGAGA CAGCTATGGC TGGAGTGATT CTCAAACTTC AGAATGTCTA

AAATCATCAC ATGGACAACT TATTAAGGAA AGCAAATGCC TGGGCTCCAT CCTCAGAGAG

TCTCATTCAC TGGGTCAGGA TAGAGCCCAG GAATCTTTAC CTTAAAGAAC CATCCCACCT

CCCACCTCAT ATGATCCTTA TGCAGGTGAT CTGGGGCCCA CACTTTGAGA AATAGACTCA

GGTCAAAGTG GCTCTAACTG CATCTCATTT CTTACCTGGC ATATCTAATA GTAGAGAAGA

AGACAATGCT AAGATTTTTG TTGGAGATCT TTTGCTGGGA TTGCTGCTTC ATTCATTCAC

TCATTTATTT ATTTATTTAT TTATTTTGAA ACAGAGTCTC ACTTTGTCAC CCAGGCTGGA

GGGCAGTGGC ACAATCTGAG CTCACTGCAG CCTCAGGCTC CTGGGTTCAA TCGATTCTCT

TGCCTCAGCC TCCCGAGTAG CTGGGATTAC AGTCATGCAC CACCACGCCC AACTAATTCT

TGTATTTTTA GTAGTGACAG CGTTTCACCA TGTTAGCTAG ACTGGTCTCG AACTCCTGAC

ATCAGGTAAT CTGCCTGCCT CGGCCTCTCA AAATTAGTAG CTGCAATTAC ACGTGTGAGC

FIGURE 6 (72)

TGCCGTGCCT GGCCTGCTGT TTCTTTTAGT TGGGCCTCTT CTGTAATAGA GTGTGAGAAT

TCTGACTTGC TGCAACAGTC TGCTTTGAAG CAGGGCTGTG TTTACACTGG TCAGATGTGG

AATTGTGGGG CACACTTAGC AGCTTCCTTC TCTAATTTTT CTGTATTTTC AGGAGAACAA

TTTTAAAAAA TTTAATAAAA ATGCCTTAAA AATTAACATT ATTATAAGAT GAATCCCATT

TTTCTAATCT TGTAAATTAA AAACAATCAT AAGCATATGA GCACCTGCAC TTAGGGAATC

AAGGTTGGCA AAGCTAAACA CTTCCAGCTC TAGGTGATTC GCGGCAATAC AAATGGAGCT

GGACTTTGGC CACAGTGCAA AAATATTGAT CTGTTGTTAG ATGCTCTGAA GTTTCCAGAA

AGAATTGGTT CTGCCTGCTG TGCTTCAGTG CTTAAGGGAA GTGGTTCCTC AAAATGTTAG

TTTTTAAGCC CAGCTTTCTT AAATAGGAAG ATTCTAATAG TAGCAAAAAT ATAAACTGCT

TCTAGGTTTA AAAAGGACCC AGCACACAAT GGTTATCACA CACCTTTCTC CTCAGGTGAT

GAGTGGATGA GTGGCCTGGT GTATTTCATA ACATCTCCCA GGTCCAAATG CTAAAGCAAT

FIGURE 6 (73)

TGCTGAAAAG ATACCATGTG TACCGGAACC TTGCAGAGGT ATTTTGTTGG CATAAAAAGA

AATATTGATC ATCTATAGTA AAAATGGTTC TACTTTAATA CTACTGAGAA AAGATTTTCT

TTTCCCAGAT CTACATCCTG AATCTTCATG AAGACAAGAT CCCCTAAACT TCCACTAACA

CCATAATGTG TGCTGTCCTT TGTAATGTAG TCCACAGATC TCATAAACTG TCAGAAATAG

CAGAGATTGT AAGGTCATCC ACTTCCCCTG TAAGGCCTGC GTCCCTCACT TACATCCCTA

ATAACGTCCT CTAACCTCTG CTGGAGGGCA GATTTAGCTG CCAGCTGGGA AGAGCTCTGC

CCTAGTCAAC ATTTTTATCT GTGGCTTTCA GATGAGAACA CTGGATGCTT ATCTGAAAAA

AGCTCCTCAG GCTGGAGGGA GGGATTGGCT CTAACAAGAT GCAATGTGAT AAGAATAAAA

GCGAAGCCAA ACTCTAGGCC CAAAGGCTCT AGCAACACAC TTTTGAGAAC CTTGGAGACG

AGTTTTGGCT GATGCGAGCT TCTCCGCCTG CTAAAGTAGC CCATTCCATT TGGACGGCTC

TAGAGGCTGG CATGTTCTTC TCCACGTTGT GTTAATGTAC TCCAGTTTCT TCCTGCCATG

FIGURE 6 (74)

AACTGGCATG CCCTGGCTCC TCCTACCTTC CCCACTTTAA GTCTTCCCTC CCTCCTTCTG

ACCTTCCCAT TCCAGCCACA CTGGCCTTTT GTCTGGTCCT AACAAACCAT GCCTTTCCTG

CCTCCAAGCC CTACACCTGC TATCCATCCC TCTGTCTGAG AGACACTCCC ACCCCTTCAC

AAAGCCTGTT TCTCATCCTT CCAGTTCAGA TGTCTTCTCA GCTTGCCTCA ACTGACCTCT

TTCAGCTATT CTCACTCTTT GTACTCTGTT CATTTCCTTC CTGGCAGTCA CCATAATTTA

TCTTTATTTG AATCAATTTC TTAGTTGTAT TATTTAGTTA TTTGCACACT CTGTCTCTCT

GTGCCTTTCT TATTCACTGC AGGCTTTCTT ATGTAAGTAA TTTATTTACT TAAATTTTTA

AAAATAATTT CAACTTTTGG CCGGGCACAG TGGCTCACGC CTGTAATCCC AGCACTTTGG

GAGGCCGAGG TGGGTAGATC AGCTGAGGTC AGGAGTTCGA GACCAGCCTG GCCAACATGG

TGAAATCCCA TCTCTATTTA AAATACAAAA ACTAGCCGGG CGTGGTGGTA TGCACCTGTA

ATCCCAGCTA CTCGGGAGGT TGAGGGAGGA GAATCACTTG AACCGGGGAG GTGGAGGTTG

FIGURE 6 (75)

CAGTGAGCTG AGATCACGCC ATTGCACTCC AGCCTGGGGC ACGAGAGTGA GACTTCATCT

CAAAAAAACA AAAAACAAAA AACCCCTGCT TTTCAGAGGG GCTGAACTAA TTTACATTCT

CACCAATAGT GTATAAGCAT TCCCCTTTCT CTACAGCCTC ACTAGCATTT ACTTTTTTAA

AAAACTTTTT AATAATAGCC ATTCTGACTG GTATGAGATG GTATCTCCTT GTGGTTTTCA

CTTGCAATTC TCTGATGATT AGTGATATTG AGCATTGTTT TATGTTTGTT GGCTGTTCGT

ATGTCTTCTT TTGAGAAGTG TCTTTTCATA TATTCTGCCC ATTTTTTGAA TGGAGTTGTT

TTGTGCTTGT TGAATTAAGT TCCTTATAGA TTCTAGATAT TAGACTTTTG TTGGATGCAT

AGTTTGTGAA TATTTTCTCC CATCCTATAG TTCTGTTTAC TCTGTTGATA GTTCCTGTTT

TGTTATGTTT TGTTTTTTTG CTGTACAGAA GCTGTTTAAT CTAATTGGTC CCACTTGTCA

ATTTTTGTTT TTGTTGCAAT GGCTTTTGAA TTTTAATAAT AAATTCTTTC CTAAGGCTGA

TGCCCAGAAC AGCATTTTCT AGGTTTTCTT CTAGGATTCT TATAGTTCAA AGTCTTATAT

FIGURE 6 (76)

TTAAGCTTTT AATCCACCTC AAGTTAATTT TTATATATAG TGAAATGCAG GGGTCCTGTT

TCATTCTTTT GCATGTGGCC AGCCAGCAAT CCCAGAACCA TTTATTGAAT AAGGAATCTT

TTCCTCATTG CTTATTTTGT CAACTTTGTC AAAGATCGGA TGACTGTAGG AGTGTGGCTT

TTTCTGGGTT ATCTACTCTG TTACATTGGT CTATGTGTCT GTTTTTGTAT CAGTATCATG

CTGTTTTTGT TACTATGGTC TCATAACATA GTTTAAAGTT GGATAATGTT ATGCCTCTGC

TTTGCTGTTT TTGCTTAAGA TTGCTTTGGC TATTGAGGCT CTTTTTTCAC TTCATATGAA

TTTTAGAATA GTTTTTTCTA ATTCTTTGAA AAATGACCTT GGCAGTTTGA TAGGAATAGC

ATTGAATCTA TAGATTGCTT TGGGCAGTAT GCTATTTTAA TGATATTGAT TCTTCCTATC

CATGAGCATG GAATATTTTT CCATTTGTTT GTGTCATCTA CTATTTCCTT TAGCAATGTT

TTTTAGTTTT CCTTGTAGAG ATCCTCCTAG GTATTTCATT TTTTATGTGA CTATTTTAAA

TGGGATTGCA TTCTTCATGT GGCTCTCAGC TTGAATGTTA TTGGTGTATA GAAATGCTAC

FIGURE 6 (77)

AGAGTTTTGT ACACTGATTC TGTATCCTGA AACCTTACTG AAGTCATTTA TCAGTTCTAG

GAGCCTTTGG CAAAGTCTGT AGTGTTTTCT AGGTATAGAA TCATATCATT AGCAAAGAAA

GATAGTTTGA CTTCTTCTTT TCCTATTTGA ATGCCTTTTA TTTCTTTCCC TTGTCTGATT

GCTCTTCCAG TACTACGTTG AATAGGAGTG CTGAGAGTGA GCATCCTTGT CTTGTTCCAC

CTCTCAGGGG AAATGGTTCC AGCTTTTGCC CATTCAATAT GATGTTGGCC ATGGGTTTGT

CACAGATGGC TCTTATTATT TTGAGGTGTA TTCCTTTGAT GCCTAGTTTG TCAAAGGCCT

TTATCATGAA GGGATGTTGG ATTTTATTGA AAGCTTTTTC TGGGTCTTAT TTGGTGAATT

GCATTTATTG AATTGTGCAT GTTGAGCCAA ACTTCCATCC CAGGGATTAA ACCTACTTAA

TCATGGTGTT AACTTTTTGA TGTGCTGCTG GATTTGGTTT GCTAATTTTT TTTTTTTTTT

TAAGATGGAG TCTCGCTCTG TCGCGCAGGC TGGAGTGCAG TGGTGTGATC TTGGCTCACT

GCAAGCTCCA CCTCCCGAGT TCATGCCATT CTCCTGCCTC AGCCTCCCGA GTAGCTGGGA

FIGURE 6 (78)

CTACAGGCAC CCGCTACCAT ACCCAGCTAA TTTTTGTATT TTTTAGTAGA GACAGGATTT

CACCATGTTA GCCAGGATGG TCTTGATCTC CTGACCTCGT GATCTGCCTG CCTCAGCCTC

CCAAAGTGGC TAGTATTTTT TTAATTACTA TTTTTTCTCA CCCTTGCTGC CATCTTATGA

TTTTCTAGTA TTTTGTTGAA GATTTTTGCA TCTATTTTCA TCAGGGATAT TGGCCTGTAA

TTTTCTTTTT TCATTTCATC TTTACCACAT TTTTGTATCA GGTTCATACT GGCTTCATAG

AATGAGTTCA GGAATGGTCC CTCCTCCTCG AATTTTCTCT GTAGAATTAG TACCAGCTCT

TTGTGTGTCT GGGAGAAGTT GTATGCCAAT AATTTAAATG CAGTTAATAT TTACTGGACA

ATTTCCTCCA GATAATTGTA TATGATTTTT GGTCCACCCT GAGTTGATAC ATGTATTTTA

ATTGTATCAT GGTATGAAAA GAGCAAGAGT TATTTGGTCA CCTAGTCTTG CCTATAGATG

TTGCCTAATG ATTCAAAGTA GATATTTTGG GAGCCTTAAC AGGTGCCGTG GACTAGGCAG

TTTTGTTTTT TTTTTTTTTT GAGGGACAGA GTCTCGTTAT GCTGCGCAGG GCTGGAGTGC

FIGURE 6 (79)

AGGGGCATGA TGTAGGATCA ATGCAACATC CGCCTCGTGG GTTCAGAGCA ATTATACTGC

ATCAGCCTCC CCAGTAGCTG GGACTACAGG CTCACGCCAC CACGCCTGGC TAATTTTTGT

ATTTTTAGTA GAGATGGGGT TTCACCATAT TGGCCAGGCT GGTGTTGAAC TCGTGGCCTC

ATGATCCACC CGCCTCGGCT CCCAATGTGC TGGGCTTACA GGCGTGAGCC ACCGCACCCG

GAGATTAGGC AATTTTATAT TCCCAAATAT CCAACTCTTC TGACCCGCTT TCTCAGCCTG

GGTGTATCAG GCACAAGGCC TGTTCAGATT ATGTGGTCTC TGAAGATATG GCTCTCCAGG

GTTGACAATG TGGATAAGGA TTCACCTGGT TTAGGATTTA CACATTCGCC TTGAATGTCT

GTTGCACCAA GTAGACAGTC CATCCCAACT TGGCCATTTG GTCAGAGCTG TAAGGAGACA

AGGAGGTGGG CAGCCGCTGC TGTGAACTGC TTGGACAAAG ACTGCCAAAT AGCTATCAGA

CAGTGTTAAC AACAGCTGAT TTAGGTTTGA AGGGGGCAGT CTCTTGGGCC ACTTACTATG

CTGCATCATC CTCTTTGGAA AATGCTCTTC AGGTAACTGC CTAACAGACT GAGAAAATAA

FIGURE 6 (80)

AATGCTCACA GAGAAAAAAG ACCCGGAAAG TCTGACTTCT CAGAGCTCAG TGTTTAGGTG

CAGAACTGGA TTGTGAAAGG ATTTTTAAAT TTTTTATATT CATTGCAGGG AACATTCATT

TATTCCATCC TTCTCCACTC CCACCTGTCT GTCGTTGTCT TTGTCTCTGT CTCCCCACCT

CTCTCTCTAG ACACACACAC GCACACACAC ACACACACAC ACACACACAC ACACACACAC

ACACACACAC ACACACACAC ACACACACAC CCCTATTCAT TGCCAACAGT AATAGAGTTG

CTTCTTTACT TCTTGGAGAG AAAAGCCTCA ATCTGAGGAA GCTGTGCTGA CTAGCCTTGC

TCTTAATCAT GGAGACAATG CTTTATGCCT TTATCTTTGC ACAGCTGAAA GCCATGGCAG

AAGCAGTCCT CTAAACGAAA TAAAATAGAA AGGTTCCTGC TAAGCCCTGG CAAATGCAGC

CTTCTATCCC TCCCCCAACA CTCACAGCTT CTGAGCAAGA TGTTGCTGCC TTCCAGGAGC

TGGGTGATGG GCAATAATGA GCAGAGCCAC GTGAAGGAAA GATGGGTGAA GAAATGTGTG

TGGAGTCATG CTGGCTGCAC TGACCATGAA ACAAAGGATC TACCCCTCTA GTAACTGCCC

FIGURE 6 (81)

TACTCCTTTG GTAACTGTTC TGAAATTATA ACTTGCCAGA AGTTCAGAAG GACCTAGTGC

AGGTATTAGA GGAAATTCGT AAGATTGAGC CATTTATTCC TGCACAGATA CATAATAATG

GACACGGGCC ATGGTGGCCA GCATTCTTGC TCTTGACAAT GGTGAAGGGA AGGGTTGTAG

GTCATGGCTA TGCTCTCAGA ATTATAATGG AAAGAAACAG CTCCTGAGTG TTTACTATGA

GCCAAGGGCT GTGCTAAACA CTTTACCATA TGATGACATC TTTTTCTCAC AGGTATCAAA

AAACAATAGG ACATACCGGA TAGCTACAAT CTTTGGGCCC CTGCAAACAC AATAATGTGT

ATTCTCTTCT TCAAATCCTA CATATTGCTA CAAACTGTAT CCCTGAGGCA TATTCATTGT

AAAATAAAAA CATATAAAGT ACTACTTTTG TTTTTTGAGA TGGAGTCTCG CTCTGTCACC

CAGACTGGAG TGCAATAGCA TGATCGTGGC TCACTGCAAC CCCCTGCTCC TGGGCTCAAG

TGATTCTCCT GACTCAGCCT CTCAAGTAGC TGGGATTACA GGCGCACGCC CCCATGCCTG

GCTAATTTTT GTACTTTTAA TAGAGACCAG GTTTCACCAT GTTGGCCAGG CTGGTCTCAA

FIGURE 6 (82)

ACTCCTGACC TCAAGTGATC CACCTGCCTC GGCCTTCCAA AGTGCTGGCA TTACAGCTGT

GAGCCACTGC ACCCGGCCCA TATAAAGTAC TACTAATGTA ACAGGGTGCT AGTCCAGACA

GTGACCACAC GTGGTGTTCA TTGAAGGCTG GACTAACAAC TCCAGCCTCT CCGCCATCAC

AGAGTGATGA CTGCCTTCCC TGAAGCAAAG CTTCTGGTTC AAGGAAAGGC CAGTAAGTGA

CTGCTCTTTG TTGTATACAT GTTAGATGAT CAGGCCTCAA GAAAAGTATA AAGAGATCTT

TGTGCTCTCT GGGACTCAAA AAGCTGCACT CTTTGGGGGA AGGATAGCCA GGTAAAAGTG

GCCCAGGTAA AGAGGGCCTG GTACACCTGG TTCTGCAAGA TGGTAGACAC AAAAATGAGA

GCTACATTTG GAGCTTATGT GCCCCTAACT CTGTACATAA CCTGCAAGAT CTAATTACTA

ACAACTGGAA TCTTGGAAAC ACCTGTAGTA CATCCTTGGC TAAGGTTAGC CCCAACAGAG

AGGGCTCTCC TCTTACAGAG AACCATTACA TTTGTGCCTT CATCCTAGAG TAGAAAAGGC

ATGATCAGAC TACTAAAAAG ACATCAGGAA AGGGCCTGTG ACATCTGAGG GAAGTGGTTG

FIGURE 6 (83)

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CCCTCTCTGG GATGTTGGTT CGGGAAGAGG GGCATGGAGG AGTGCCTGCT TTAGATGGTC
ATTCAGGAAC CCAGGCTGAT AGTGAGAGGT GAAGCCAGTT GGGCTTCTGG GCTAGGGGGG
ACTTGGAGAA CTTTTGTGTC TAGCTAAAGG ATTGTAAATG CACCAATCAG CACTCTGTAA
AATGGACCAA TCAGCAGGAT GTGGGCAGGG CCAAATAAGG GAATAAAAGC TGGCCACCAG
AGCCAGCAGT GGCAAACTGC TCAGGTCCCC TTCCACGCTG TGGAAGCTTT GTTCTTTTGC
TCTTCACAAT AAATCTTGCT GCTGCTCACT CTTTGGGTCT GCACTATCTT TATGAGCTGT
AACACTCACC GTGAGGGTCT GTGGCTTCAT TCCTGAAGTC AGTGAGACCA CAAACCCACT
GGGAGGAACA AACAACTCTG GACACGCCAA CTTTAAGAGC TGTAACATTC ACTGCGAAGG
TCTGCGGCTT CACCTCTGAA GTCAGCGAGA CTATGAACCC ACTGGAAGGA AGAAACTCCA
GACACATCTG AACATCTGAA GGAAGAAACT CCAGACACAC CATCTTTAAG AGCTGTAACA
CTCACTGCAA GGGTCTGCGG CTTCATTCTT GAAGTCAGCA AGACCAAGAA CCCACTGGAA
```

FIGURE 6 (84)

GGAAACAATT CCGGACACAT TTTGGTGACC CAGATGGGAC TATCACCAAG TGGTGAGTAC

CATCAACCCC TTTCACTTGT TATTCTGTCC TATTTTTCCT TAGAATTCGG GGGCTAAATA

TTGGGCACCT GTCAGCCAGT TAAAAGCGAC TAGCATGGCT GCCAGACTTA AGAAACTAAA

GACACGGGTG TCAGACTTTC TGGGAAAGGG CTCTCTAATA ACCCCCAACT CTTTGGAGTT

GGGAGCGTTG GTTTGCCTGG AACCAGCTTC CACATTTCCT GTACTTCTGG GCTGAGACGA

GGGTCAACAT AGAGGAAAGC CATTCAGCTC TGGGGTCCCG ACAGCAAGTT GGTTGACCCT

GTGGCCATGA TCACAACTCT CGAAGTCATG TTGCCCAAGC GAGACTCACC CATCTATCCT

ATCTATCCTG ACTCTTGCTT CCTGGGTCCT AATGCCTGGA AGACAAAACT TCCTCTTGTC

TCTGTTCTCC AAGGCTAGTC CCACTTCTAA AAACCACTCC CTGTCTCTGG TGCTTTTCTA

GTTTCTCCTA TAAGAATGAT TTCTAGTATA AACTCCAGGA CTCTATTCTC TTCTTTAGGC

ACCCGGGCTC ACCAATCAGA AAGCCATAAT TTTTGCCCAA AGCCCCATCT TAGGGGGGAC

FIGURE 6 (85)

TATCTGGAAT TTTAGGATCC CTCCTCAGAC AAGCAGGCCT AACAAAAGCT ATTCCTGAAG

CTAGGATATG GGGAGCCTCA GAAATGATAT CCTTCCTATT CAAGTGAGGA CAAAAGGCAT

CACTCTTCCA ATTCTGGAGA TCCCTTCCCT CCCTCAGGGT ATGGCCCTCC ACTTCACTTT

TGGGGCATAA CGTCTTTATA GGACACGGGT AAAGTCCCAA TACTAACAGG AGAATGTTTA

GGACTCTAAC AGGTTTTCAA GAATGTGTCG GTAAGGGCCA CTAAATCCGA TTTTTCTCGG

TCCTCTTTGT GGTCTAGGAG GACAGGTAAG GGTGCAGGTT TTCAATAATG TGTTGGTAAG

GGCCACTAAA TCTGACATTC CTTGGTCCTC CTTGTGGTCT AGGAGGAAAA CTAGTGTTTC

TGCTGCTGCA TCAGTGAGCG CAACTATTCC AATCAACAGG GTCCAGGGAC CATTGTGGGT

TCTTGGGCAA GAGGTGTTTC TGCTGCTGCA TTGGTGGGCT CAACTATTCC AATCAGCAGG

GTCCAGTGAC CTTTGCGGGT TCTTGGGTCG GGGGGTGGGG GGAACAAACA GACCAAAACT

GGGGGCAGTT TTGTCTTTCA GATGGGAAAC ACTCAGGCAC CAACAGGCTC ACCCTTGAAA

FIGURE 6 (86)

TGTATCCTAA GCCATTGGGA CTAATTTGAC CCGCAAACCC TGAAAAAGAG TGGCTCATTT

TATTCTGCAC TATGGCCTGG TCCCAATATT CTCTCTCTGA TGGGGAAAAA TGGCCACCTG

AAGGAAGTAT AAATTACAAT ACTATCCTGC AGCTTGACCT TTTCTGTAAG AAGGAAAGCA

AATGGAGTGA AATACCTTAT GTCCAAACTT TCTTTTCATT AAAGGAAAAT CCACAACTAT

GCAAAACTTA CAATTCACAT CCCACAAGAA GAACTCTCAC TTACCCCCAT ATCCTAGCTT

CCCTATAGCT CCCCTTCCTA TTAATGATAA GCCTCCTCTA TCTCCCCACC CAGAAGGAAA

CAAGCAAAGA AATCTCCAAA GGACCACAAA AACCCCTGGG CTATCGGTTA TGTCCCCTTC

AAGCTGTAGC GGGGGAGGGG AATTTGGCCC AACCCAGGTA CATGTCCCCT TCTCCCTCTC

TGATTTAAAG CAGATCAAGG CAGACCAGGG GAAGCTTTCA GATGATCCTG ATAGGTATAC

AGATGTCCTA CAGGGTCTAG GGCAAACCTT CAATCTCACT TGGAGAGATG TCATGCTATT

GTTAGATCAA ACCCTGGCCT TTAATTTAAA GAATGTGGCT TTAGCCACAG CCCGAGAGTT

FIGURE 6 (87)

TGGAGATACC TGGTATCTTA GTCAAGTAAA TGATAGAATG ACAGCTGGGG AAAGGACAA

AGTCTCTCCC GGTCAGCAAG CCATCCCTAG TGTGGATCCC CACTGGGACC TAGACTCAGA

TCATTGGGAC TGGAGTCGCA AACATCTGTT GACCTGTGTT CTAGAAAGAC TAAGGAGAAT

TAGGAAAGAG CCTATGAATT ATTCAATGAT GTCCACCATA ACTCAGGAAA AGGAAGAAAG

TCTTGCCTTC CTTGAGTGGC TACAGGAGCC TTAAGAAAAT ACACTCCCCT GTCACCCAAC

TCACTCAAGG GTTAATTGAT TCTAAAAGAT ATGTTTATTA CTCAATCAGC TGCAGATATC

AGGAGAAAGC TCCCAAAAGC AAGCCCTTGG CCCTGAACAA AATTTGGAGG CATTATTAAA

CCTGGCAACC TTGGTGTTCT ATAATAGGGG CCAAGAGGAG CAGGCCAAAA TGGAAAAGCG

AGATAAGAGA AAGGCCACAG CCTTAGTCAT GGCCCTCAGA CAAACAAACC TTGGTGGTTC

AGAGAGGACA GAAAATGGAG CAGGCCAATC ACCCAGTAGG GCTTGTTGTC AGTGTGGTTT

GCAAGGACAG TTTAAAAAAG ATTGTCCTAT GAGAAACAAG CTGCCCCCTC ACCCATGTCC

FIGURE 6 (88)

ACTATCGCTG AAGCAATCAC TGGAAGCCAC ACTGCCCCAA AGGACAAAGA TTATCTGGGC

CAGAAGCCCC CAAGCAGATG ATCCAACCAC AGGACTGAGG TGCTCAGGGT TAGCGCCAGC

TCATGTCATC ACCTCACTGA GCCCTGGGTA CATTTAACCA TTGAGGGCCA GGAAATTGAC

TTCTACTGGA CACTGGTGCG GCTTTCTCAG TGTTAACCTC CTGTCCTGGA CAGCTGTCCT

CAAGGTCTGT TACCATCCGA GGAATCCTGG GACAGCCTAT ATCCAGGTAT TTCTCCCACC

TCCTCAGTTG TAACTGGGAG ACTTTGCTAC AGATAGTAAG TATGCTTACC TAATCCTACA

TGCCCATGCT GCGATATGGA AAGAAAGGGA ATTCCTAACT TCTGGGTGAA CCCCCATTAA

ATATCACAAG GAAACTATGG AGTTATTGCA CACAGTGCAA AAACCCAAGG AGGTGGCGGT

CTTACATTGC CGAAGCCATC AAAAGGGGAA GGAGAGGGGA GAACTGCAGC ATAAGTGGCT

GGCAGAGGCA GGGAAAGACA AGCAGAAAGG AAAGAGAGAA AGAGCAGAAA GTGAGAGAGA

AAGAGAGATA GGAAGTGATA GCAAAGAGGG AGTCAGAAAG AAAAGAGAGA GGAGAGAGAG

104/285	115/285
105/285	116/285
106/285	117/285
107/285	118/285
108/285	119/285
109/285	120/285
110/285	121/285
111/285	122/285
112/285	123/285
113/285	124/285
114/285	125/285

FIGURE 6 (89)

AGGGGGAAAG ACAGAGAGAG ACAGAGGAAG AGACAGAGAG ACAGAAAGAG AGAAGCAAAG

AGAGGAAGAG ACAAAGAAGG AGTCAAAGAG AGGGAAAGAG AAGTAGTAAA GAAAAAACAG

TGTACCCTAT TCCTTTAAAA GCCAGGTTAA ATTTAAAACC TATAATTGAT AATTGAAGGC

CTTTTCTGTT AACCCTATAA TACTCCCAAT ACCACCTTGT TGTTCAGTGT TAAACAAGGG

TTATTAGCCC AAAAGCCACT GAGGCCACTG ACAACCCGTA GCCTTCTTAT CCAAAATCCT

TAACACAGCA GGTTTCCTAA CAGGGATCTA ATCTTAGGTC GACCAGACTG GAGAACTGCC

TTCAGGACAG GATGATAGAT GGTTCCTCCC AGGTGATTAA GGAAAAAGAC ACAATGGGTA

TTCAGTAAGT GATAAGGAAA CTCTTATAGA AGCAGAGTTA GGAAAATTGC GAAATAAGTG

GTCTGCTCAA ACGTTGAAGC TGTTTGCTGT TTGCACTCAG CTAAACCTTA AAGTACTTAC

AGAATCAGGA AGGAGCCATC TATACCAATT CTAAGTTAAT ATGGACTGAA CGAGGTTTTA

TTAATAGCAA AGAAAATTAA AATCTCAAAC TTACGAGGTT TTCAAGTAAA GTAAAGTTTG

FIGURE 6 (90)

GTAAAAGTTA ACAGCGTAAC ATGTATTATC CTAGTACCAC ACATTCTCTC AAAGGATTTG

CTCAGACAGT TTGCAAAAAA GAACGAAATC TGTCCTTACT CTACAATCCC AAATAGACTT

TTGGCAGCAG TGACTCTCCA AAACCGCTGA GGCCTAGACT CTCATGTTGA GAAAGGAAGA

TTCTGCACTT CTTAGGGGTA GAGTGTTGTT TTTATACTAA CCAGTCAGGG ATAGTATGAG

ATACCACCCA GTGTTTACAG GAAAAGGCTT CTGAAATCAG ACAATGCCTT TCAAACTCTT

ATACCAACCT CTGGAGTTGG GCGACATGGC TTCTCCCCTT TCTAGGTCCT GTGACAGCCA

TCTTGCTAAT AGTCGCATTT GGGCCCTGTA TTTTTAACCT CTTGGTCAAA TTTGTTTCCT

CTAGGATCGA GGCCATCAAG CTACAGATGA TCTTACAAAT GTAACCCCAA ATGAGCTCAA

CTAACAACTT CTGCTGAGGA CCCCTGGACC GACCCGCTGG CCCTTTCAAT GGCCTAAAGA

GCTCCCCTCT GGAGGACACT ACCACTGCAG GGCCCCTTCT TCACCCCTAT CCAGCAGGAA

GTAGCTACAG CGGTCATCGC CAAATCCCAA CAGCAGCTGG GGTGTCCTGT TTGGAGGGGG

FIGURE 6 (91)

GATTGAGAGG TGAAGCCAGC TGGGCTTCTG GGTCAGGTGG GGACTTGGAG AACTTTTGTG

TCTAGCTAAA GGATTGTAAA TGCACCAATC AGCACTCTGT GTCTAGCTAA AGGATTGTAA

ATGCACCAAT CAGCACTCTG TAAAATGGAC CAATCAGCAG GATGTGGGCG GGGTCAAATA

AGGGAGTAAA AACTGGCCAC CCGAGCCAGC AGTGGCAACC CACTCGGGTC CCCTTCCACA

CTGTGGAAGC TTTGTTCTTT TGCTCTTCAC AATAAATCTT GCTGCTGCTC ATTCTTTGTG

TCCACACTAC CTTTATGAGC TGTAACACTC ACTGCGAGGG TCTGTGGCTT CATTCCTGAA

GTCAACAGAC CACGAACCCA CTGGAAGGAA CAAAGAACTC CCGATGTGCT GCCTTTAAGA

GCTGTAACAC TCACTGCGAA GCTCTGCAGC TTCACTCCTG AAGTCAGTGA GACCACAAAC

CCACCAGAAG GAAGAAACTC TGGACACACC TGAATATCTG AAGGAACAAA CTCCAGACAC

ACCATCTTTC AGAGCTGTAA CACTCACCGC AAGGGTCTGT GGCTTCATTC TTGAAGTCAG

CAAGACCAAG AACCCACCGG AAGGAACAAA TTCCAGACAC AGTAGGAAAT CTGTATTTTT

FIGURE 6 (92)

GATCTGTGGC TTCCAGGGTT ACTCCAGTCA TTGAAGTCTC CATTGCAGCC TTAAGGAAAC

AGAGAATGGT TTGGAGGAGC ACATGTGGGA ATTGTTATGG ACCAGGCTTG AGATGCACAT

AGGGCATTTC TGATCAAACC TAGCTGGAAG CAGGGCCAGG AAATATAATC TAAGGAAGAC

AGTTTTTGTA GACAGTAGTA GTCTTTGCAT CTGAGACATG TAGATTATCA AGCAATTAAT

TAGAAAAAAT ATAGCCAGGT GCGATGGCTC ATGCCTGTAA TCCCAGCACT TTGGGAGGCC

AAGGGGTGTG GATCACGAGG TCAGGCGTTC GAGACCAGCC TGGCCAACAT GGTGAAACCC

CGTCTCTACT AAAAATACAA AAATTAGCCT GGTGTGGTGG CACGCATCTG TAATCCCAGT

ACTCAGGAGG CTGAGGCAGG GGAATCTCTT GAACTTGGGA GGCAGAGGTT GCAGTGAGCC

AAGATCACAC CACAGCACTC CATCCTGGGT GACAGAGCGA GACTCTGTCT CAAAAAAAAA

AAAAAAAAAA GGAAAGGAAA ATATAATCAA GAATATTGAC AGGTAACATT TATTCAACAC

TTACTATGCA CCAGGCAATA CACTAAGTGT TTTACATGGA TTAACTCATT TAATCTTAAC

FIGURE 6 (93)

AATAGCCCTA TGAAGTCAGT GCTGTTATTA TCTCCACTTT ATAGATAAGG AAACTGAAGT

ACAGAAAGGT CAAGTAGAGA AATGGCCATG CTTGCATTCT CAGTTTTTGA AGCAACTGTT

ACAGGAATCT GGTGTGAGAA ATGCTCTAAC AAGATGTGAG TCAGGGGTTG GGAGGTACTG

AGTCTGAGTT GGGCAGTTGG GGATGGAAGG ATGGATGAAG AACAGCTTGA CAGAGAAGCT

GACACTTGGC AACTCTGTGG GACCTTGAAG GGTTAGAGGG ACTTCACCAA AGAAACTGGT

GGTCAGGGAT ACGGGAGGGT CACGGCAAGG AGGGAAAGGA AACTGTACCA CAGCAGAGAG

TCTGAAGCTA CTACAGTGTA GTTCAGCGTA TAAAGAATAA TTATTTTAAG GTAAACTTAT

AACCTCATGC AAATATAAAA TGAACACGTG TCAAAGATCT TATTTAATTT ATTAATTAAT

GAGGGAACCT GTAAGATGTT ACAGCCAGTT CAAAGGATAA TTCAAATAAA TCCATGCACA

TATGTAGGCA ATAAGGAATG CTGAAATGAA TTTAAAAGTA GATGTAAACT GATTTATCCA

CAGAGAAATA ATCAGTTGCA TTTCACATAA CAAAATTCAG TTGCTTTTCT ACAGAAGGAA

FIGURE 6 (94)

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TTGTTTGCAT CATTACCAAT TTTTCTACAA CTAACAGAAT TATAAAATAA CTCAAACACA
ATGAAAGGCA GATATAACCC ACAATGGTAT GATAGATACA ATATCCACAT CCAGGATGTT
TTTTTCTCAT TTCAAAGTCT TTCACAAGTT TTCCTGATAA GGGAGTGTCA ATAATACTGT
ATGGCAGGCA ATAAGACTGG ATGGATGGTT GGGGCCAGGT TTTAAGGGGT AATAAATGCC
ATGTAAAGGT ATGTGCATAC TGTGCAACAT GTCGGGGAAT CTCAAATTAT TGGTAGAGTA
TGTAAGAAAC ACTTGTGGAG CTTGTTAATA AATTCAAATT CCCAGACCCA ACTCCTCAAG
GGTCTAATAC AGTAGGTTTG GAGTAAAGCC TGAAAATCTG CAATTGTGCA AAAAAAAAAA
CCCAGGTGAT TCTGATACAC TTTGAGAAGC ACTGGTGGAA CTAATAGTCA CTGAACGTTT
TTGAGCAGGG GAGAAACCTG AGGACGTCTA TGTTGCAGCA GTGGAAACTT GATTAGAAGT
AGGAGAAGAT GCATGGTCTT AAAAGAATGC AAAATGATGG CTAATATTTG AGTGCTTATG
ATGGGCCAGG GGCTGTGCTA GGCGCGTGGC ACACATTCAA TACGATGGAA GCCTGTACCA
```

FIGURE 6 (95)

GTCAGTATTA GTGGGGTATC TTTAAGAGTG ACCAGAATTA AGGGGGGTTT TCACCAAAGC

CTGAGGACTG AGCCTCCTCA TCCTAAATTC AGACACAATG CTGTACCTAT GCATTTGCCT

CCAGGCTGTT CCTGGGCCTC CAGGGACTGG CCCAGGCTCC TGATAAATAG GGACTCCCAA

CAACATAAAG CCTGGATTTT GGAACTTCCT GAATGTTACT CAGGCTTTCT AGTAACTGTG

GAGATCTGAA TAATAACACA ATTCTAAGTT CCCCTACTCA TAAAGCTGCT CATCATTTAG

ATGGGGTAAA GCACCTGAAA TACAATGAGC ATCACTATTT TCATTCATCC ATGAAATGAA

CATTCCGGGG AGATCAGTAA GTTGATGTAT CACCCTTGAA CAGGGCAAAA TGAATACTCA

CCAGGAATAT GTGGTATTTT AAAAAGAAGG CAAAGGGAAG AATAGTGGGG ATGGGGCAAA

AACTTTAAAT AGATTCCCCC AATCATATAT GGCAATTGAA GATAATTAAA TTATCATTTT

AATTGAGTAA GTACTCATAG AGCCCTCACT ATTTGAAAAT GAACTGCCTC CTAATTGTTA

TTGTGCAAAT GTGATACATT AAACTTAAGC TATTTTAATA AAACATCCAT TTTCGGAAGC

FIGURE 6 (96)

TGTAGTAGGT TCTCCCAGGT CAGATTTGAT AAGCCATAAA GAACAAATGC CAACTCCTAT

TTTTCTATGG TGCTGGGAAA TAAGAGAGAA ATGTGTAATT CAAAGCAATC ATTTAATTTT

ATCCAATAGC TTGATTCTCC TCTCTCTTCT AGCCTTTTAG CTAAGCTGTT ACCAAGTAAC

CACACTAGTT GGCTTGAGTC TTACCACTGT TTCCCTGACC CCACAGTGGA GAGACTGCAT

CTGTTAAAGA GCAGTTATGT AACCATGGCT ATGCTGAGCT GGGATTCCCA AGGCTTAGGT

TCTTTCTGTG AATGACCTTC ACCAAGACAC CTGAGGTCTG TGTGGAACCA CAGGCTTGTC

ATCTCTAAGG CAGAGTTGAT AATTCCATCT GTTTCTTGAG CCCACACTGA GAAAAAGATT

ACATGACTGC AGTTATTTGA ATGCCTCATG GAAAGACGTC TTATAAATAT TATAATTAAT

GTTATCATTA AGTAATGCTT CAATGCAGAT CTTCCAAGTA TAAATATCAG CTGAGTAAGA

AGTCAATCTT CCCTGAAGCA AAATTGAAAT TTGTAAATGC GATTTCTGGG AGCTTATTTT

GTAATACATG ATTCCAGAGT GTCCATAACA CACACAATTG TCTTTTTTCC CCTACATGGG

FIGURE 6 (97)

CTATTTACAA CAAAATTGGA CTTATAATGT TTATTTCCAG GGATGACTAG AACTTTAATA

ACAAACCTTG GGCCAGGCAT AGTGGCTCAT GCCTATAATC ACAGCACTTC GGGAGGCTGA

GGCTGGTTAG ATTACTTGAG GCCAGGAGTT TGAGAACAGC CTGGCCAACA TGGCAAAACC

CTGTCTCTAC TAAAAATACA AAAATTAGCC GGGTGTGGTG GCGCATGCCA GTAATCCCAG

TTACTAGGTA GGCTGAGGTA CGACAATCGC TGGAACCTGG GAGGCGGAGG TTGCAGTGAG

CTGAGATTGC ACTACTGCAC TCCAGCCTGG GTGACAGAGA AAGACTCTGT CTCAAAAAAA

AAAAAAAAAT AATAATAATA ATAATAAACC CTGATGAAAG GTTTCTAAAA TGTTTTCATC

TAATGGTTTT CTTGACAATT AAATTTTCTA TATAATGTCA GTTCATAAAA AAACTGAGAA

CGACCACATG TCATATCGAC TGCTTAAAAG AAAATACGTA TATTTACAAA CATATACACA

ATACTGTCTT TTGTCTGGTT AGTTTAGAGG TTAGATAAAC TGCAGTATGT TGTAGTGGAC

AGATCATAGA ACTAGGAGTC AGGATGTCTG GATTCCTAGG AAGCAATGAA TAGGTTGCAC

FIGURE 6 (98)

GGTGCAGCTC AAGGTTATTC AAAGTGTGGT GCCCAGACCA GCATCATGAG TATCCTCAGG

GAGCTTGTTA GAACTGCAGA TCCTTTAACT CATTGAATCA GAATCCCTAG GTGTGGGGCC

CTGAAATCTG TATTTTAGCA GGCTCTCTGG GATTGTGATG TGCCTTAGAG TTTGACAACC

ACTGGGTAGC TGATCCTGAC TTAGACTTAT CAGGCATGTG ATCTTGAACA AGTCACATAA

TCTCACTGAG TTCAGTTTTC TTATGTTTAA AATAGGCCCA ATAATATCTA TTTCACATGG

ATTGCTTTGA GGATTAGGCA AGAGATCTGT AACAGACACT GTAGAACAGT GTCTCTGGTC

TACAGCTGAC CTTCCATAAA TGGTAGTTGC CTTGATTCTC TGCTCTGCCA CATAATAGCT

GGTTAACTAT GAGCAAGTAA TTTAGTTCTT CTCAGTTTAG TTTCTTCCCC TGTAAAAGAA

GGAAAATAAC TGTTATACTC CATTTCTGAA TTGCTATAAA AGTCATTTAA TTATGGGCAT

TGAAGCTCTT TGTTCACTGT ATAAGGACTG TACATCTAAG GGATTAATGA GACCAGGCTT

ATGATTTTAA GCATGGAGTA AATAGTAACA CTGACTCTGT TCTATGAACC ACATGGAAAC

FIGURE 6 (99)

TCTAAAGAAT ATGCACATTT GAAACACAGG TATCATCTGG GGAAGGTGAT CTGCTCACCC

AAACCAGTTC ATGAACATCA ATCTCCAGTG GCGTGCTGGA GCTAGCTGTA CCAGCTCATG

AGGGCCAATT GTTTCATTTT TAGGAATTTT GTTTGCTGGT TAAAAATAGT CATTATTTAA

AATTAAATTA TGTAAACAAT AATATTAGAT AAAATAAGTT AAAATAAAAA CAAAGGAACT

AATTATCCCC AAACTCTTCC CCACCTAATT ATTTTACTAT CTGTGCCTTG GGATTATTTA

CATTGATTTT ATCCATATGG TGACAATACT ATTCATATAT AAATGGTGTG CTTCTCTTCA

TAACTCTACA TAGCCTGATG TCAGGCTAGT AGCTTGAAAT TGGCCACAGT GGGAGTGTGA

GCATTTGTAC CATGAGGCTT GGCCAAGGCT ACAAATCCAG ACTTTTGTTT TTCCCTCCTG

GAGAGCTGTC TGTTAAAAAT TTACCAACAC ACCACTGGTC TTACCTTTGT TAATTTACCA

CAGTCCAGGT TCTGACCTAG ACTTAGAAAC CTGGATTTGT CAGCAAGCTG AGGATAGAGC

CATTATTTCT AAGAAGGACT CACATTACCC AAGTGCAAAG CCTGATATAT ACCTTCAGAA

FIGURE 6 (100)

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TATCAATTTA TTAATTTACA GTGAAGAAAG CCACCCCAGG GCATTCCCCA GGGGAAGGCA

AAAAGAGCTA GTTGCACATT TTGAATGTTT GATGACATTA GGGTAAGGTG ACACAGAATA

TCCATTTCCA CAACTGAGAT ACCTGCTGCC TTAAGGAAGG GACAGGCAAG TCCTTGGGCA

GGACCTTAGA TTGTCACTGT CCATCTTGCT GTAGGACTCT CCTTTCCAGG CATGACGATG

GCCAACTCTG TCCTCCTACC CTACTGATGG GATTATCTTT TCTTGACACA TGGCAATGCC

TCCAATCAGA GGCTGGTAGC TATTTTTAAT CTTCAGGGCA GTATTTTTCA AAGGGAAGTT

CATGGACCAT ATGCATCTGT ATCATTTAGA TGTATATTAA AAATGCTTAG TCTTCCCCAG

TTATACTAGA TCAGAATCTC TGTTGGTGGG GCCCACGAAT CGGTATTTTC AACAAATCAC

TAGGTAATTT CTGTATATAC TATAGTGTGA AGACCACTGC TTGAAGGTTT CTTTGCATAT

CTCCACTAAA TATAAAAAAT ATTGACTTCT AGATTTAACT CCCAAAGCAC TTGCATTTTT

AAGTTTCTGG GGGCATTATA TTGTGGTACC CCTATACCAC TCACACTCTA GTCAGGAGGT
```

FIGURE 6 (101)

ATATTATGGA CTGAATGTTT GTGTCCCTCC AAAACTCATA TGTTGAAGTC TTAGCTTCCA

ATGTGATAGT ATTAGGAGAT GGTGCCTTCT GGAGGTAAAA TCAAGCCCTC ATGAATGGGA

TTAGTGCCTT TAGAAAGAGA GCTCGTCACT GTCTTTCCAT CAATTGAAGA TGCAGTGAGA

AGCTGGTAGT CTTGCATCTG GAAGAGGGCC CTCACACAAC CTGATCATGC TGGCACCTGG

TCTCAGACTT TCTGCCTCCA GAACTATGAG ATGATAAATT TCTGTTGTTC ATACCCCACC

CAGGCTACAA TATTAGGTTG CTGCAAAGTA TTTGTGATTT TTGCCTTTAC TTTTCAGGGC

AAAAACTGCA ATTACTTTTG TGCCAACCTA ATATTTTGTT ATAGCAGCCC GAACTAAGGC

AAGGGAGACT ACATCAGACA GTGTAGCTAT GTAAGTACAA ATGTATCCCT GTTGAAGGAA

AACTAAGTTC TAACCCTGAC TTCAGGCCAG TAGCCACCTT TTCAATCTCT TTCATGAAGG

GACCATTATC ATTATCACTG GTGGCAAAAA TAGAGCACGA GAATGGAATT TGCTTTTCTG

TGAAATCTCA GTGTATACAG ATGAAGAGCA AGGGTTTGCT TTCATCTCTA AGAAGCAAAA

FIGURE 6 (102)

GTGAGTACGG ACTGGCACAT TATCAGAGAA AGAATCATTC TAGCTCGGTG GGTCTTAACC

AGGAGTGAAT TTGACTCCAG GGAACAGTTG GCAATGTCTG GAGACGTTTT TATTTGTTAT

AGCTGGGGGA TGAGTGGGTG GGTTGCTACT GGCATCTAGT GGGTGGAGAC CAGAGATGCT

GTTAAACATC CCGCAAAGCA CAGGACAGTC CCCGACAACA AAGAATTATC TGGCCCCAAA

TATCAATAGT GCCAAAGTTG AGAAACCTCA TTCTAGCTTC CTTTTCCCTT CTACGTTCTA

ATCAACTGTT GTTCTTTCAG CATTAGGATT CATCCAGCAG TCTCTTTCCC CAGCAATTTG

TTGAAATTTT TTTAAAAATG GACTCATTTT AGTGTCACAA GAAAAAAATA CATTCACAGG

AAAGGATGGG TCATTTTGTT TAATGATGTT TTGCCTTTCA CATAGCAAAA GCTTAATAAA

GTATTTTTAA ATAAAATGGT GAATAGATCA AAACATTAAT TTCACATGTG TTTTAATAAA

TAACAGGAAG ATGGCTATAT TATATAAATT GTTCTTGTAT ATGTCTTGAG TGGATCATCA

AACACAAACG TATCTACATG CCTTTTCTTG TGAATAGATC TAATAATAAC GCTCTTCTAA

FIGURE 6 (103)

AAACAAATTA AATGGATATT ATTTGCTGAG AATGTAATGC TTGTGTGAAT AGAAGCCAGC

CCTGAATCCA AGCCCCCAGA TCTATTTAAA GAATTTGAAG AATGTCAGAA AAGCACGTGG

CTTCAAGGTT AATGTGTAAG ACTCACAGAA ACTTGAAAAA TCACTATGAC TAAAAAGAAA

GTATGAGCTC CCTGCATGCC TGTAAATTGG AATGACAGCC AAAACCAGTT AATTATAAAA

ACAGCTAATT TAACAGGTTT TCAAATTTGT TTCTTTCTCC AAGTAGCATA TAGTCAATAA

TCCTTAAAGA GAAAGCAAAG AAGGGGAAGC ACTGAACCAA ATTTGCTTTT TTGTACCTGC

TCAGCTCAAA TGCAGAGTTC TCTACCTGGA AATTGACTGC TTCCATAGTT TGATAGCCAC

AGAGAGATGG GAACAGAAGG AGAGGTATAA TCCCAGACTT GATTCAGCTA TAGAGAATGA

CAATAGTGTC AGAGGCCTTC CAACCAGAGC GACTCCATCT TGAATACGGG CTGGGTAAAA

CAGGGCTGAG ACCTACTGGG CTGCATTCCC AGGAGGCTAA GCATTCTAAG TCACAGGATG

AGACAGGAGG TCAGCACAAG ACCTTGCTGA TAAAACAGGT TGTAATAAAG AAGCCAGCCA

FIGURE 6 (104)

AAACCCACCA AAACCAAGAT GGCCATGAGA GTTATCTGTG GTTGGTCTCA CTGCTCATTG

TATGCTAATT ATAATGTATT AGCATGTTAA AAGACACTCC CACCAGTGCT ATGACAGTTT

ACAGGTACAT TGGCAACTTC CGGAAGTTAC CCTCTATGGT CTAAAAAGGG GAGGAACCCT

CACCTCCCAG AATTGCCCAC CCCTTTCCTG GAAAACTTGT GAATAATTCA CCCTTGTTCA

GCATATAATC AAGAAGTAAC TGTAAGTATC CTTAGGCCAG AAGCTCAGGC CACTGCTCTG

AATGTGGAAT AGCCATTCTT TTATCCTTTA CTTTCTTAAT AAACTTGCTT TCACTTTACT

GTATGGACCC CTGTGAATTC TTTCTTGCAA GAGATCCAAA AACTCTCTCT TGGGGTCTGG

ATCAGGACCT CTTCCCAGTA ACAATAGTAG TAAGGGGTCG GGGAAACTGG ACAAAGGAGT

TTAAGAAGCC TTAGATAAAG GGTCCTCATC ATTGTCATAA CATAAAATCA TGGACTCCTA

GAATTTTATA GCTGATAGGA TTAGAAATTT CAAAATTCAA TTTCATTAAT TTTCATCTGC

GAAAACAGAT GGCCAGAGAG GCCAAACAAT TTGTTAAGGA GCACTGAGGC GATGGAACAC

FIGURE 6 (105)

CACACTGGAC CGCAAACCTC CTAGCAGAGT ATACAAGGCC TTTGATCTCC TCAGTCAGAA

TGAACTAGAG CTTTCCAGGG GTACCCTTTC TGACTGTTTA GCATGTTTGC CAGTCTGACT

AATTTTGAAG TTGCTTAAAT ATCTGTCATT TCCACTGTAT CATAATCTCC TCATTCATCT

TCAATCTCCA ATGCCTTGAA CTCAGTAAAT GTTAGTTGAA CAAAAGTAAA TTGAACCCAG

AATTTCTGAT CATAATCTGG AGCACTTTAA AATTGTCAGC TTACTGGGAA ACGGGATAAC

ATGTGATTTG TCTTTGATTT TTTTTTTCTC ATATGCTTTT TCCACCTATA GATGCTACAC

GAATGTTTTT AAAATCTGAT ATAAAAATTA AAATTAAAAA ATTAAAAAAA GAAAATTTGA

TACAATGCTA CATTTAGAGT GTTGTGATTA GATTCCTTAA GTGTATCATG GTGATCTCTA

CATCACGTGG TGATCAAATT GCTTTGGGTT TTAACACATA ACTGACAAAG GCTTGGGGAC

ATGTAAGATC CCAAATACAT TTTTATTGAT TTTTTTTTCT TGTTTGTCCT CTTTTAAATA

ACTTTTTTTT GTTATAAGAA TAATTCATGT TCAGTGGAGA AACCATAGAA AATAGTGACA

FIGURE 6 (106)

AGTGAAGGAA TAAATTTAAA ATGACCCATA ATTGTACCAT ACATTCTGAT TTTTTAAACG
CTGAACAAAT TAGCCTTGGG TAAGTACCAG GAATAGAGTG CAGCATTGAA AGTTAAAGTT
TGGGGAAGGA TAGCTGACTT AAGAAATTAT CTAGTTAGAC ATTTTTTGGA TGGGGTAATT
TTGCAGATGA CATTAGTGAG AGAAAGGACT TGCCACTCTC ACACAGCTAG TAGGGGTGTG
GGAGGATATT GGAACCAAGT TTCAAGTCTT CAGTGAAGAA TCAAGGGAGA AGTTCTAAAA
CCTAACAATA TCCCTCTGGA TGGACATTTA TTTTATTACT ACAATAAGCC ACACGGTGAG
TCATAAGGAG CATTTCATTC TTCTAATATG TCTCTACTGT ATTTAGAATC TGATAAAGCC
CTATTAGAAT TCATCTCTTT AAGAATAAAA GAAGCTGAGG AACTAAAGAG AGGGTTGGAA
TAATCCACTA ATTATATCCG TTAAGCTTCA GTTACGCTAA TAAGGAATAT CACATGACTG
TGGTGTGTGC TTGTTCTGAA CAGTAAAGTA CATGAGGAAA GATAAGATTC AGGGCTGAAA
TGTCCTTCAG CATATGTAGG TAGTGGTGAT GAAAGTCATT AAAAGAAAAA TTGATTGAGG

FIGURE 6 (107)

TATTTTAGTA AACAAAAGAA CTCACCACTT ACCCATCAGG AAGTGTATTG TTAATGCAGT

GCTGTTCAGC CTTCTGGAAG AAAAGGTTTC TTCATGCTTC TCTCTTTAGC CTAATTCTTA

TCCTGTCACT TTTCAGGCAA AATTAAAAAA AAAAAAAGAT TGAAAACGAT GCTCCTATTT

TATTTGCTTC AAAAGAAACA GGCTGTTGCA TTGTGCTTGG AACAGTTTAC TCTTGGCCTT

GATGTAAGTG TGAAAGGAAG CCCATGTAAT TGACTAGGCA GTATCTGAAG AAGCAGGAAA

TACAGTGTTA AGAAAATGAA CAGGCATGAA AACCATGGCT ATTTGATAAA AGTAAATAAT

TTCTGCAGTT CACATGTTCT CAGCATATTT TCTTTGATAC TGACTTGCTT AATATGACAA

TAGCAGAACC ATGGTAGCTT GTAGGCATTA CTTTTCTTTT AATTTCTTTT ACATTTTGAA

TTTACCAGCA CTCACATTTG TATTACTTTT GGGTTATACT GAGGATCTAT AACTTATAGA

TCAAATACCT GACATATATA TGCATTCTCT GAAGTCTTAG GGCAGAACTA GAACATTCTT

GTGAACATCA GTATAAGATA TTAAAATGGA AGTTTTGCCT AAGACTGAAG ACAATAAAAA

FIGURE 6 (108)

TATCATAGTC TGAAATGAAT GCCAGCACAC CATACAGGAT TTAAATATCT ATACATATAT

ATGTGTGTGT ATTATATATA TTTAATATAT ATCTGTGTGG GATAGGAAGA GGTAGGGGGA

AATCAGTTTT ACAATTATTA AGTATTTCAC CCTTGACAAG AGTATATATA TTGGAAATCA

GTTGGAGAGT ATTTTCAAAG ATAAATGTTA GTGTGCTATG AATGAATCCA CCCCTACCAC

CACTGAGGCA GGGTAGGAGA GGCCTGTGCT CCTCAAGCAT AGTTGGAAAA GGACCTCAAC

AAGACCACTT CAAGAGTCTA ATGTGTGGAG ACTGTTGCTT AGGGAGACCT TATGGTCTAG

CTTCTGACTC ACAGCTAAGT CAGGGAGACA GGTTGGCTGC TCTGATCGTG GAGTCCAAAA

GATGGCCTGC ACTGAAAAGC CTCATGAGTG TTGACTTAGG GCTAGTCTAA GAGGTCCCTG

GAAGAAGAAA CACTCAGTAG GAGAGAAGCT GGAGGTACCT TCAGTGCTGA ATTGGAACTA

GATTCATTCC CCCGTGGAGC AAATTACATA GGAAAGATGC CCAGTGATGG AGAGTGGGGG

TGTCTCTAAC AATTACCCAC CCACTGCCCC CACCCTAAGA AAAAGAAAAT CACATACAAC

FIGURE 6 (109)

CAGTCAGCTG TAAACATATG CCGAGCCTAG TAAACTCAGA TACTAAGTTA CCAGGGTACC

TGGCAAGTAA GAACATTCCT GATTCCCTTC CTCTCTTCTC TTTGCCCTCC AACCTTAGTG

GCTAGCAAGA TGGGGAGAGG AGGAGAAGCT GTAAGTGGGG AAAAAAGAGC AGCTTTCTCT

CCTTTTCAGC TGCTGGATTC TCCCTCATCA TAGGCCTGAG CTGGGGAATC AGGAAGAAGG

ATTCTTTTTA AAACTGAAGT AACGTTATCA TTTAATTTTA AAACATTTTA AATTTTGACA

ATGTTGAGAT TAGATATACT AATTATTAAA CTAAGATTAT GTTTTGCAGC TTGAAGTGAT

AAGAAAAACT CTTATCTAAG AGCATCCAGG AAAGTCGGGG GTTTCCTGAA CATCCTTTTA

AATCCTTTGG AAGTCAGCTT TCAGAGAGGA TTTAAAGTGT AGACTGGGCC TTCAGAAACT

TGGTTAATGT AGGGGTTTCC TATGCAGACT TGGGGACTAT ACCTTGTGTG GAAGAGAGAA

AATAAGATTA TCTTACATTT TTCCCATTCC TTTTTCAAAA AGAAAGCTCA GCTAGCATGA

AAGTTAAATT CAAAACGTAA TGGGTATTAT TTGCATATTC AAATCTAGTG CATATCATGT

FIGURE 6 (110)

AAGTACTGAA TTATGGTATT CATTATTTCA AATGACAAGC TGGATTTTTT TTTCTTTCGA

ATTTCACAAA TTAATTTTCC TTGGAACCTT TTGGTTTGGG CTTTAAGAGT TTAGGCTTTC

ATCACAAAGA GAGGACAGCC TTGAAGATTA AAGTGTGTGG CTCTTCTCAA GATGTTCTTA

GTCCAGCAAA GGATTCTATG CATATTTGGG CTTCCTTCTG TCTCATAACC TGTATTTCTT

GATATTCTAT TTATATTCTG TAAGATTTTT TTTTTAAAGG AAAAATTCTT CCATGGTTGA

AGGACATGTC AAAAATAGAG GATACAGTTT TATATCAAAG GAAGTTTCAT GATATGACTG

TAGAAGCTCA TTTGACTTAA GACACATCAT TTCCTCATGG AAGTGTTAAA CAGATCTGTA

CAATAAGGTT GGCAATCTTT GTGTAAAACA GTTTTTTTTC TCCTGCTCTA AAGAAAGTGT

ATATTTCAAA ATGTGAATGT CAGCAGTCAG AAAATAGTAT TTTTTTAACT TCGTTTTCAA

AGTCCTCAAA AACCTGTACC TAATCATGAA TTTTTTTTCC CACAGATTGT TTCTTCTTCT

CCCTCCCAGA AACTTTGAAG TTTTTCTACA TGACACCAGG ACCTATGTCT TTTTTTAATT

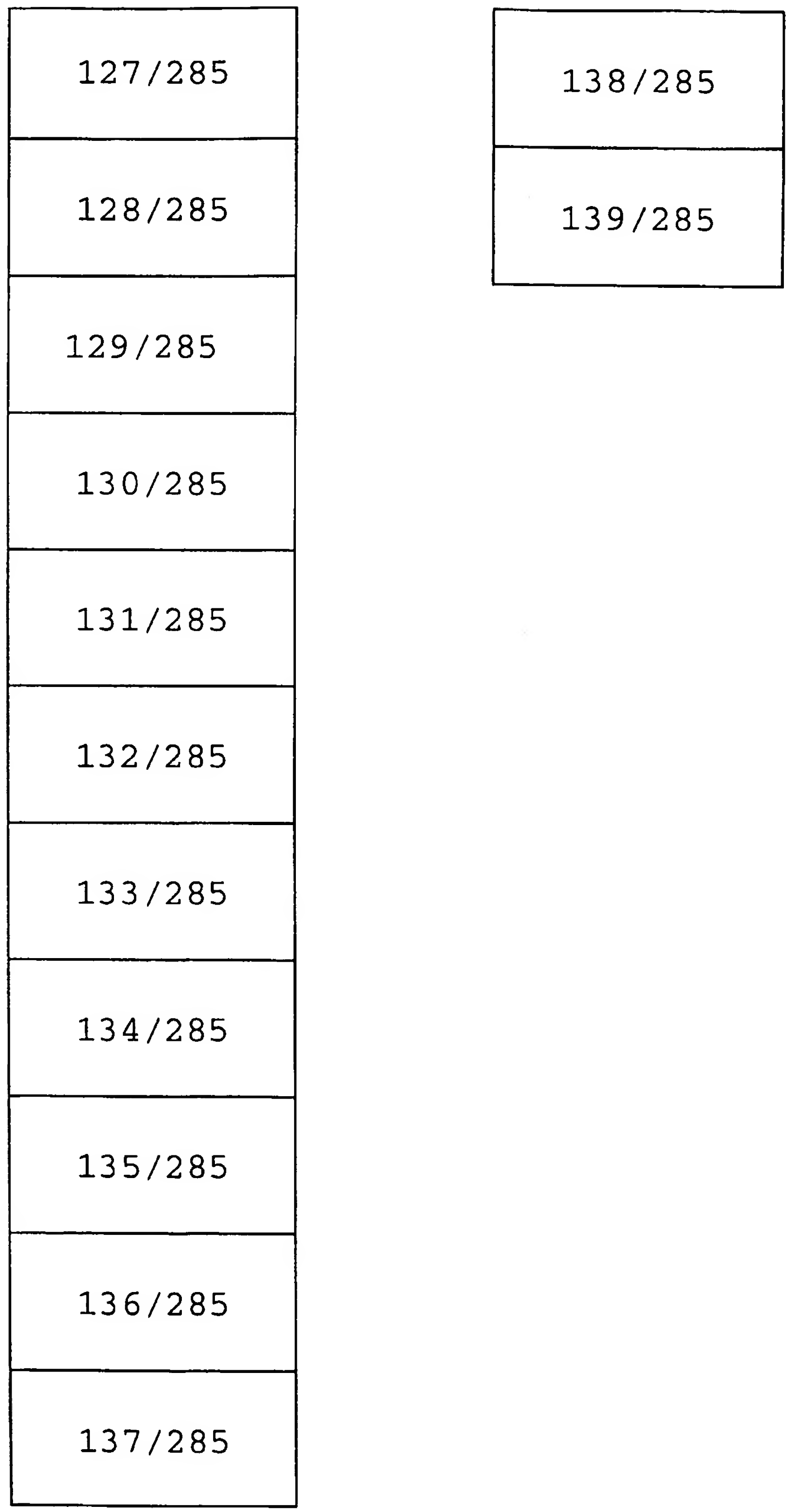
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FIGURE 6 (111)

ACACAGAAAT GAAAGAAAAA AAGTGTGTTG TATCGTTAAC CAAATATATG AAATCTTTAA

GCTGTATTTT TATTTTTAAC TTTGTTTTGC AAAGAGGCCA TTCCCTTTGG TTAAATAATT

TGTTATTCAC AGTTTCCTTG TCCTCATATT ATCAAGGGGA AAATTGTAGA AATTTTAAAG

GAAGCTCTAG GCAATGTTTT CATCCCTGAA TCTTTGGAGA GTTATAAAAA CAAACAGATT

ACTGAACCTG TAAGAGAACC AATCGTGAAG TCATTACATC TAAGCATAAG CAAAATCTCC

TCTTGGATCA TTAAGTTATA GAAGAAAAGA AAGCCTGCAC TTTGAAATTT AGATAAAGCT

TGGTAACTTG TAAGTCAAAC ACGTAAAATT TTACAATTCA GGAATATCGA TAGCAGTTGA

GTTTAATAGA CTTCTCACAT TCCAAATTTA AAGCTTCCTT CTCTGTGCTA ATAGAGATAC

AATAGCAGTA GGCGTTTAAG AAGAATGAAT CAACAATTTA AAACTATAAT GTGTTTTTTA

TTCATCTCCC TTATTCACAT ATATTTGTTT TGTTTTGAGA AGGAGTTCTG CTCTGTCGCC

CAGGCAGGAG TGCTGTGGCA CGATCTCAGC TCACCGCAAC CTCTGCCTCC CGGGTTCAAG

FIGURE 6 (112)

CGATTCTCTT GCCTCAGCCT CCTGAGTAGC TGCGATTACA GGCGTGCGCC AGCAACCCCG

GCTAATTTTT GTATTTTTAG TAGAGACAGG GTTTCACCAC GTTGGACATC TTGGTCTCGA

ACCCCTGATC TCAAGTGATC AGCCCGCCTC GGCCTCCCAA AGTGCTGGGA TTACAGGCGT

GAGCCATCAC TTCTGGCCCT TATTCGCATA CAATTTAAAA ATCATCACAG AAGGTTTGAA

AGAAGGAAGG GGCAGAAAAT TACCTACTTT TCCTCTCCCC AGCGATCTCC TTCAAATCTG

TGCCTTTTCC TCAGGCCCAG GCCTCAATTT ACTGAGCAGT CACACCTCAC AGAGGGAGGT

CTGGGCAATC CACTCTTGGT CACAGGAAAG CCATTGACCC TCCCACTTCC TCTCCTCCAC

CTTGTTCTCA ACTCTTGACT TTGGGCTTTG TTTCTGTTCA AGTCCTAGAA CTGGTTTCTT

TTATCAGGTT AAGTGATTAG TTCTCTTTCC CTCTAGTTGC TCTCACTCCC TGACTCTTGC

CTTCTGTAAC AACTGGAGAC AACTCTTTCA AAACCAGCTC CAAGCCCCAG ACTTCTCTCT

GGGCTTTAGT TCGTAAGGCA GGTGCCCTAC TGAGTGAGCC TAGATCAGAC AGAAACATAG

FIGURE 6 (113)

CTGTTGGCAA GGATTTAGGT GAATTTCCTT CCATTGTTTT TCTAATACCT TTTTTTTTTT

TTTGTAAATA TAACCATGCA CCTACACACA TATTTGAATA TCCTGCCTTT TTATTTAAAA

TGACATGATA GGTCCGGGAG TGGTGGCTCA TGCCTGTAAT CCCAGCACTT TGGGAGGCCG

AGGTGGGCAG ATCACCTGAG GTCAGGAGTT CGAGACCAGC CTGGCCAACA TGGTGAAACT

CCATCTCTAC TAAAAATCAA AAATTAGCCG GGCATGGTGG CAGGCTCCCA GCTACTCAGG

AGGCTGAGAT GTGAAAATCG CTTGAACCCG GGAGGTAGAG GTTGCAGTGA GCTGAGATCT

TGCCATTGCA TTCCAGCCTG GGCAATAAGA GCGAAACTCC ATCTCAAAAA AAAAAAAAAA

AAAAAGACAG GATAAACATT CTAGATAGTC TCTATAATGG TCATGATTAA GACAATAAAA

TAGTCTGAAA TTGTCAATAT ATATTAATAA TAATTTATTT GGCCATTCTG CCAAGTAGCA

GACACCTGTC ATTCTGCCCA CTCAGCACCT CTCTTTCTTT TAGGGAAATG CTACCCACTC

TTTGCATGGG TTCTGGATGG AACTGTTGAT CACAGTGTTT TCACTCCCCA TTTTGCCTCA

FIGURE 6 (114)

CCAGAGGTAG ACAGAAGACC CAAGCCAGGC CAGTTACACA CAATCTTCAG ATAATTACCG

TATTGATCAC AGTATCACCC CACTCAAGGC TTGGTTGGAG ATGAGCAGAA GAGACTAAAG

CTGGGTCATT TTAATTAACA CCTGTACCCC AAAGAAAGAC TGTCAATGAG GCTTTTATAC

CGACACTCCT GGTTTCCATT CTTCCTGATG CCATTCATTT GACGAACTAC CCAATCTTTC

CAACAGTGTC TTTGGAAGAA AGATAGTCAG AAAAGAAGAT AGAGTTGTTT TCTGTTCTTT

GCAACCAAGG AACTCTAAAT GATAGACTTG TTGCTAGGCA CTTTGGTTAT TTTTATTATC

TTGAATACTT CTGTGATATA CTTCTTTGTG CATGCCTGTT TGTACGGATG TAGCTTTTTA

TATATTTTAT ATAATTTCTC AGAAGTGGAA TTACTTAGTC AAAAGGTATG AACATTTTCT

GATTCTTAAT ATAAATTGTG CAAATGCTTT TTAAGAAGAT TATACCAGTT TACATTTTGT

GTTATATATA ACAGAAAGTA CTACTGAAAA ATATTACAAA AATTGTCTCT CTGTTCAGGA

GGACTTGTAA TAGATGATAA AGTACTTGAA ATAGGAACAT AGAGCATTTT CAGTTTAAAA

FIGURE 6 (115)

```
TAATTTCATT GGGTTATTTA CGGAATCCTT AGAATTATGG CCAGACATTT ATAGATGATC
TGTACCAAAC CTAGTTGGTT ACATAAATTG CTTATTCAAC TGGCTTAAAT CTATAATAGA
AAGATGACAC TTACTGAATG TTTAATATAC ACTTTGTCAG GGGCTTTGTA TTATTCTATG
ACATCTTCAA AATGACCCTA CTTTCCTATT TTATAAGTAA GGACAGGAAG GCTTCAAGAA
CATGACTAAT TTTCCCAAGG GCTGTACCAA AGCCAGAACC CAAATCTATA AGGCTTTTAA
ACCTGCATTC TAAAACTGCA TCTCGGCCAT CTTATTCCTA CAGAACTTAA GGTTAGAAAG
CCAGATTGGA GTCCCAATTT CACCACTTAG TAACCAGACA AACTTGAGGA ATTCACTCAA
CGTCTTTGAA TCTCCATTTC CTAATCTTTA AAACTAAAAC AATAATACTG GCCCTACCTA
TTTCCTAAAA TTTCGTGAGG CACATAGAGC TAGTGTGGTA GAGTGCTGTA CAGATGTCAA
GTGTTAGCGT GAATTACTTA GATCCCTGAA CACCATGGAT GAATGTGTCT GACTGCTATT
AGAGGTCATA AAGAATATTG GGGCCAGGTA CATTGGCTTA TTCCTATAAT GCCAGCACTT
```

FIGURE 6 (116)

TGGGAGCCTG AGACAGGAGG ATCACTCGAG GCCACAATTT CAAGACCGGC CTGGGCAACA

TAGTGAGACC CCTTCTCTAC AAAAAAAAAA AAGCAGCCAC GTGTAGTGGC ACACACCTGT

AGTCCCACAT ACTCAGGAGG GTGATTTGGG AGGATAACTT TAGTCCAGGA GTTTCAAGGT

GCAGTGAGCT GTGATTGCAC CACTGTACTC TAACCTGGAC AGCAGAGTGA GACCCTGTCT

CTAAAAAAAA AGAAAAAAAA AATAATAATA ATAAAGAATA ATGGGCCTTG GGATACCCAC

TCCTCTCTTT CTGCTCTGAG TTGTGAAGCA GTTGAGTTAC ATATGCATGT CCAATGGATG

AGGTTGAAAA TATCAACTGG ATTGGAATGT GGCTTACTTG CGTGGCCACA ATGAGCTTCG

TAACACTTCC TGACAGGGTG AGAAGACAAA CTTCCTCACC CAGTCACTGG CAGAGCTGGA

CACTCTGTGT CTCTCCCACA GAACAACCTC TTACTGCATG GAGGTGGATG AAAAAGTCAA

CCGAGAACAG GCTACTCCAA AAAGCAGAGC ACCAAAGGCA CCAGCTGGTC AGGTCCCCCT

TCCTAAGTAA ACAATCACGT AATTCATTCG GGACAAAGCC AGAGAGGTGG TGTGGAGAAA

FIGURE 6 (117)

GAGAGGGCAG TTTCCTCCCA AGTTTTTCCT GGAATTCTTT ATGGGAATAT GAGGTTTAGG

GGAATAAGAC TTCCCTTTAA CAGTGAAGAA TCCCCAGCTC TATTGGTAAT AGGAAATCGC

TTACAAGGAT CATGGGGAGT ATTTCCTCAG CTCGTTCTGC CTCCTACTTG GCTGAGTGGA

ATGGAACCAT CTGTGGCTGC TGCATATGAT ATTGTCAACT TTGTCATTCC ACACCCACTC

CTTGACGCCC TACCATGTGG TCATAAGACT CCCTTTAAAG TGTTCCTTTA AAAAACAAAA

TGTGTTTTGT TTCTATAAAA TACAGCTCAA TGTCAGAACC CTTGTCTTGT TTGCTCTCTG

ATGTAACCCT TTCACAATGT TTGGGCAGCT TATTCTCTCT ATTTCCCTGT AGGGTCCCAT

CCAGGCCAAA GTGAGTGCCA GCCTCATTTG GGCAGCACAT GCCCTGTGGA AGGGCAGGAA

GAGACGAAAG CTAATTGTAA CTTTGTGATT AGCTGTCATG GATGCCTGGT CCTGTCAATA

GCGCTCAATA AAGCCAGAAG GCCAAGCGTT CGCTTCTGCA TACTGATTGC TGAGTCAGAT

TTCTCAGTGC AGAAGGGCTT TCTAGGCAGT CAATTTTAGA ATATTAGTCT TGGTTCTTAA

FIGURE 6 (118)

GTGGTTAAAA TCCCTAGCTG GTCTTTAATC TGAGCCTGGA GAATTTAGTT AGGGCTGACA

TTCTGCTGTG ATATTTTTGC CCTCAATATA TATGTCTTTC CTCCATCTCT TAGATCCCTG

AATCATAGAG ATATATATGT TATATAATCA ACTGTCTCCA GTCTCTAAGA GTGATAAGTA

CACATTGTGT CAGGTTGAGG GGACAGGAGA ACTTTCAAAA GCCTTTCTTG CCCCTTTTTC

CTTCTCACTG CCTCCCACTA AGTCCAGCCA CTTATTATTC AGCTGACACT ATCATCATGA

CCATGAGTCT TTTGGGGCTA CCCTGGTTCG GATCCTTTTG GAGGTTTGTT GCTTAACTCT

GTCTTCAGTC CTATGGAGCT GCTTTTTCAA TAAGTTTCTA TTTTGGCTAA AGTTGGCCAG

AATCTCCTTG TAACCAAAGA ACAAATAAAA TACCAGCTTG CAATGTTCTA TGTTGCTTCC

ACCAAACTTA TGCAGCACTT CCTATCTAAT CCACCTACTA GTCTTTTTTT TTTTTATTTT

TTTGGAGACG GAGTCTCGCT CTGTTGCTCA GGATGGAGTG CAATGGTGCA ATCTCGGCTC

ACTGCAACCT CTGCCTCCCG GGTTCAAGCA ATTCCCCGGC CTCAGCCTCC TGAGTAGCTG

FIGURE 6 (119)

GGACTACAGG TGCATGCCAC CACGTCCGGC TAATTTTTGT ATTTTAGGAG AGAGAGGGTT

TCACCATGTT GCCCAGGCTG GTCACGAACT CCTGAGCTCA GGCAATCCGC CCTCCTCGGG

CTCCCAAAGT GCTGGGATTA CAGGAGTGAG CCACCTCACC TGGCCCCGAC CTACTAGTCT

TTAGTGTTTG CTTCCTTCTA TTGGGTAATT GTCTGTTTAT ATGCATGTCT TGTTTCCTCA

AATAAAATGT GGTCTTCTCA AGGGTATTGG CCCATGTTCT ATCCATCTGT AGATATCACA

GCACCTAGCA GTGTCTTTCA CAGAGGAAGT ACACAACTGG CATTATTGAT TCATTGCTCC

ATTTTTTCCT TCTTTATCCC CAGCATTTCT CAATAATTTC AAACATCTCC ATTGGAGTAC

CGGAGAAAGC AGGTAGCTTT ACTTGCAGCT ATGTTTCTAT CCCCATAGTA ACTAAAAGAG

GACCCAGAGA AACATGTTTA AATGCTGTCC TGTTATCAGG ACCTCAGCCT TCTGATGCTC

CGTGGCTTGG GGGTTAATGC TTGATCATTT CCTCCCCAAC CTACACTGTG TACCTATGCT

AGTCTCTTCA TGAGGACTAA GCCCCATAGT AAAAGGGCTA GATAAATAGA AAATCATTTT

FIGURE 6 (120)

ATGTAATTAT AAGAATGAGA ATACTGAGTA TTACTGGTGT TTGTTTAGGA TAAGCACATC

TTTATTTGTA TGAGAAAAAG AAAAAGAGAG TGAAAAATAT ATTAACGTGC ATATAGTTCA

GGACCATGGA TTGCAAGTGA CAGAAACTCA ATTCAAACCA ACGTAAGTCA AAAGGAAAAT

ATATTGGCTC ATGTAACCTT CTCACAGAGA GGGCAGGATG GAAGGGGCTT TGGGAACAAG

AGAATTGTTC TCAAATTCTA GGAATACTAG GATTAGTCCA GGATGGGTCA CCTTCCTGTC

CCTGAGGTGG TGGTAGCGAT GGTAGAGTCT TATGGGAGGA AAGAGTGCAT GTTAGGATGA

AGGTAGGGCT AAGCAAACAA GGGCAAGGGC CACTATATCA TGCTAAAAAT GGTTTTTTTT

GATGTCTTCC TTAATTTCAC AAATGCTTCC AACAAAGTAG CACACAGGAA AAAGAACATA

GGGACTCTAC TGGTGGGTGC TTTTATCTTA AGCCTTGTAC TTGCTTTTCA CAGCTTACTC

ACTGCTTGTA CCTGAGGCCA TATGCCCTGT AAAAGCTTCT GCAGGGTTTC TACTAAGCTG

GGTTCCTTAT ATGGCTCTCT CCCATTTCTG TTGCCTCACT CTAGTGATCT TTCTCTTTTC

FIGURE 6 (121)

CTCACCTCTG GGACTGGTGG CTGTTTGTAT GGACTGCCTT AGCTTTGCTT TGGGTTTTTT

CCTGGGGACA ATGTCTTCAG ATTATCCTAG ACCAAATAAA CTACAGCCAC TGGGCCAGGC

TCTTCCTCCT CCAACTGGAC CATGTTCCCA GGGCTCTTCA CCTTAGTTTA GGTCAAGCAT

TCTTGGCAAA AGAAAGGCCT AGTTAACAAT AGACATTCTA GCAATTGATT CTTTTTGACA

TGTTGTAAGA TCTATTCACA TTTTGTAATT AAAGCATTCC CCTATGGAAA CCAACACGAA

CTAAGCTGCT CCTGGAATGC AGGGTGGCCT CCTCAATACA GGATGTTCTA GAGAGCTGTA

TTTTGGGCAC TTAACTATTC TCCACTACTT AGGGCACAGC ACTGAAATTA ACACCACTAA

GTTTGTCATG TCCATGTAGT TAGTCTCAGG CAGTGCAGCC TCAGGAGTGG AACTGACCTC

TTATGTGTGT CCAGCCTTTC TTCCTTCAGA AGTCAGCTGT GTTTTCTGCT GACTCTCCAT

AGGAACATCA GTCCTGAATC CTCAGACCAC CATCTGGAGT AGTAAGTGCT CCTGACAGTC

CTAGAAGTTG TCTACCGCTG GATCTCCAAA GCGTGTGACA CACCGTGAGA GAGAAATGAG

FIGURE 6 (122)

AAAGCTGGGC TCTTCAGGTA AATCTTGCTT TTTCACAAGC CCCCTAATTT TACTGCATAA

TTATTTTGAA TTCACTGATA ATTTCTACAA TTTTCCCATA AGTCATCTAC ACACAATACC

CTCTCATGCA ACACTTGGCT TTGCTAATAC ATATCTATTA TGAGAGCTGT GCTTCTTAAG

CGTAAATGTT TTATATGCAC TAAGGCTCTT GGCTTACATA TAAAAGGGGT ATTGAGCAAT

GTGATACAGA AGTCTTTTCT CCACAGGTCT CATATGTAAA GAATTCATTA GATTGGCTGA

AATAGACTGA TCTGTCCATT TCTCTGCTCA CTTATCATAA GGAAGTCATT AGCTAAGGAA

CAAAAACTAC AATCTATGTA ATTAGAAGAA CAAGCTGGTT TTGCTCAATA TAAAAATAAG

AAAAAGAAAC CATGTGAAAG TCAAAATATT TGTTTAATCA GGTCATTGAG AATCTATTAA

AAAGTATTTG AATTCTTTAT GATGAGAACT ATCTTGACTC AAGTGGACAG TGGTGAGCTT

TTTGGCCTGT GGTCCCTACG TAGAAAGGAG GCTTTGTCAT AAAGTCTTAT ATGGTACAGG

TGCCAAGTTA AGTGCCCAAG CTTGCTCTTA AAAGCATACT GGATTTTGTT TTAGACTTTT

FIGURE 6 (123)

AGTGAACTGA AGGGAATAAA CAAATCCCTC TGGGAGAACT TCTCCTCCAT CCTTGGTGAA

GTCATTCTGC CAGAATTC

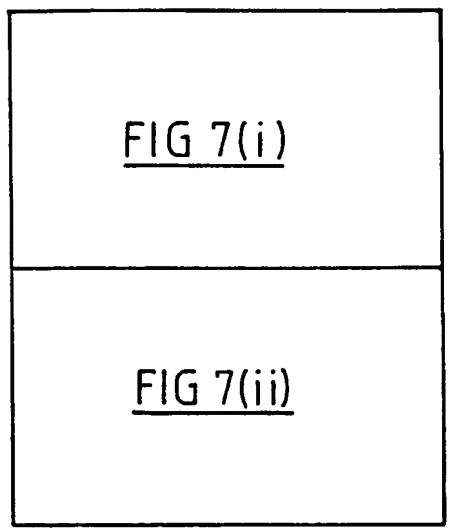


FIG 7

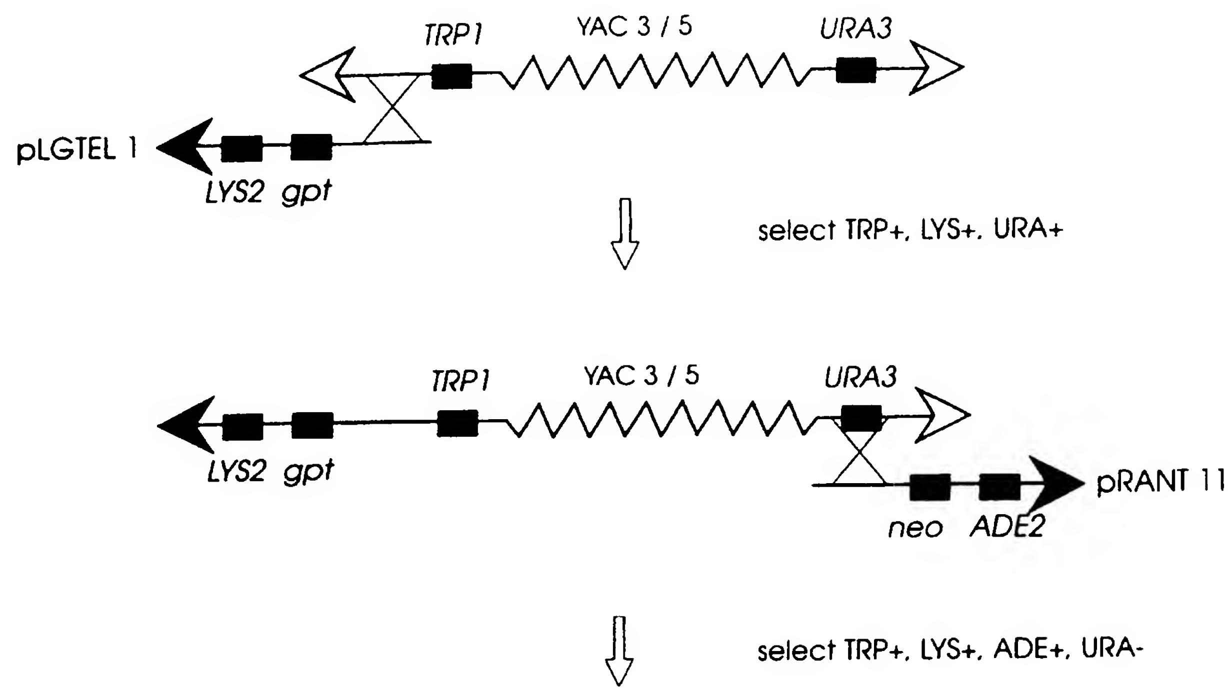


FIG 7(i) Procedure used to retrofit YAC 3 and YAC 5.

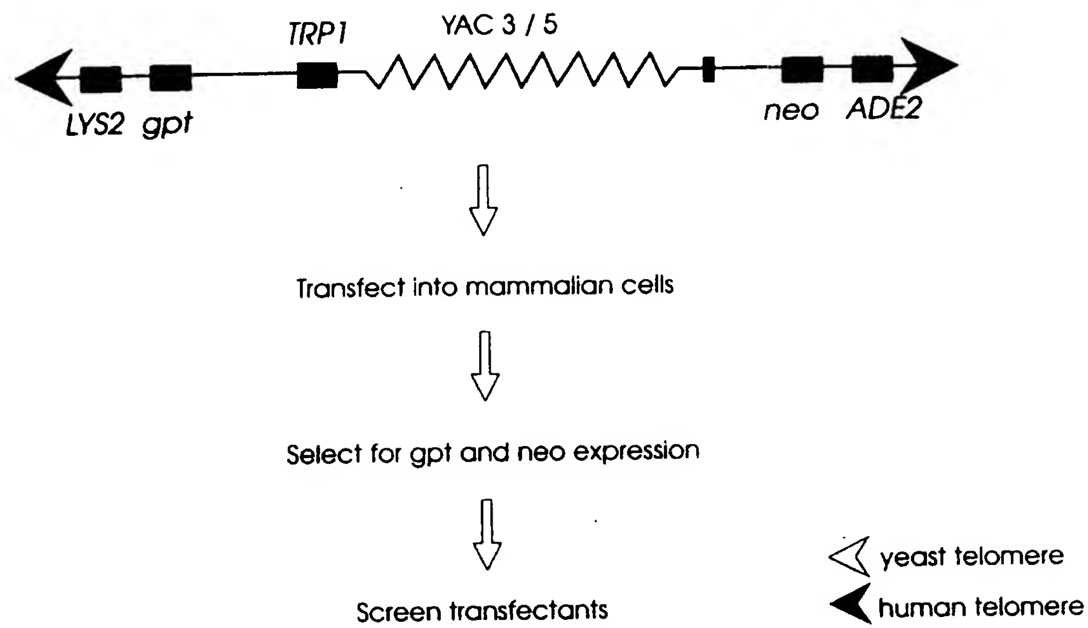
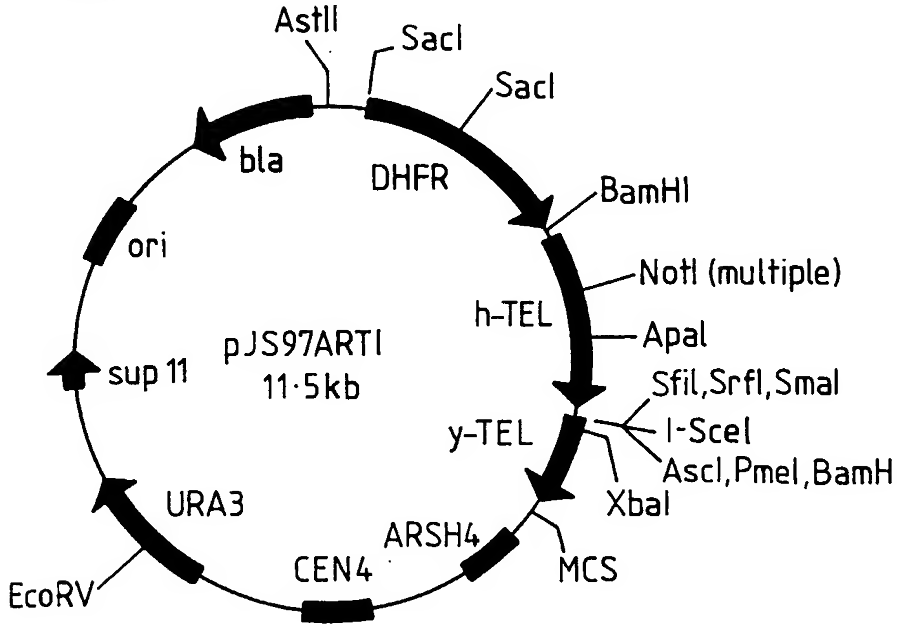


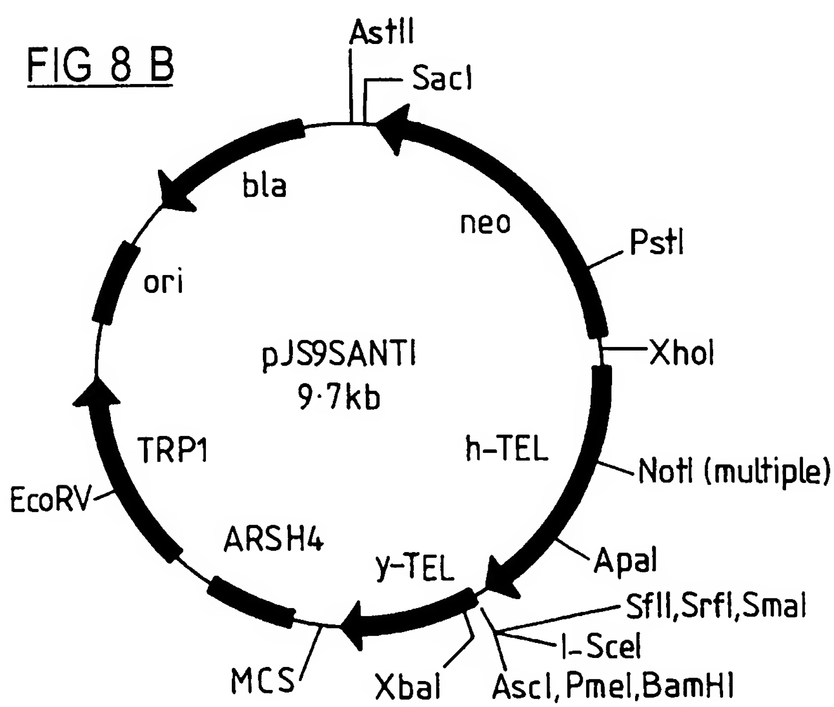
FIG 7(ii) Procedure used to retrofit YAC 3 and YAC 5.

FIG 8 A



MCS = T7, EcoRI, BglII, NotI, XmaIII, SstII, SalI, NruI, NheI, BstBI, ClaI

FIG 8 B



T7, EcoRI, BglII, NotI, XmaIII, SstII, SalI, NruI, NheI, BstBI, ClaI

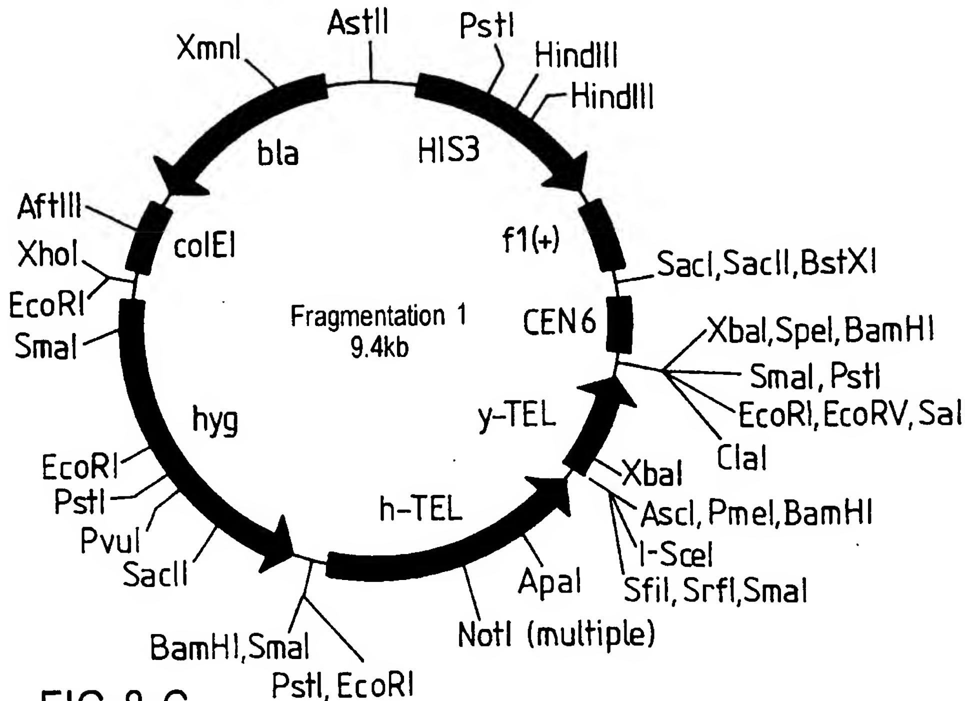
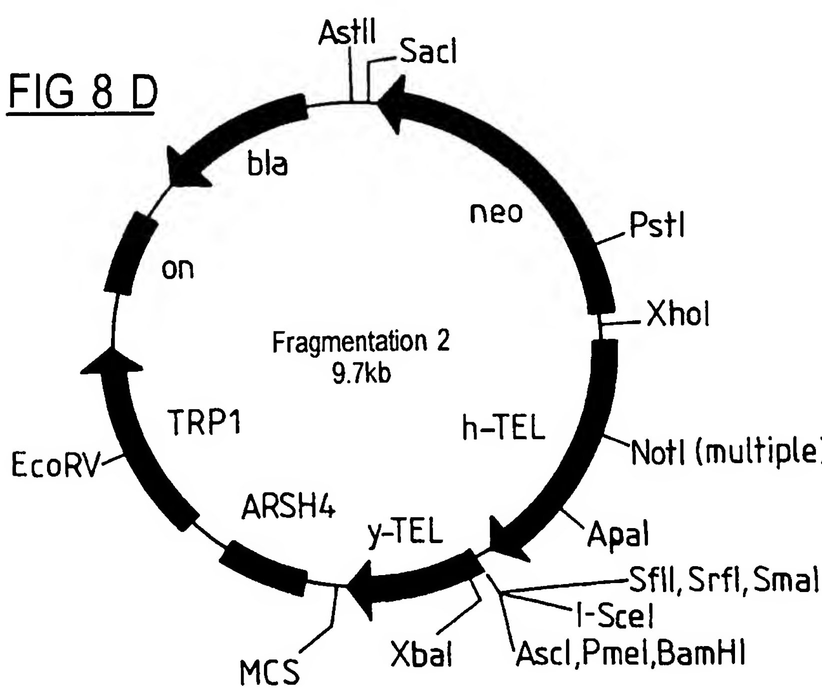


FIG 8 C

FIG 8 D



T7, EcoRI, BglII, NotI, XmaIII, SstII, SalI, NruI, NheI, BstBI, ClaI

FIG 8 E

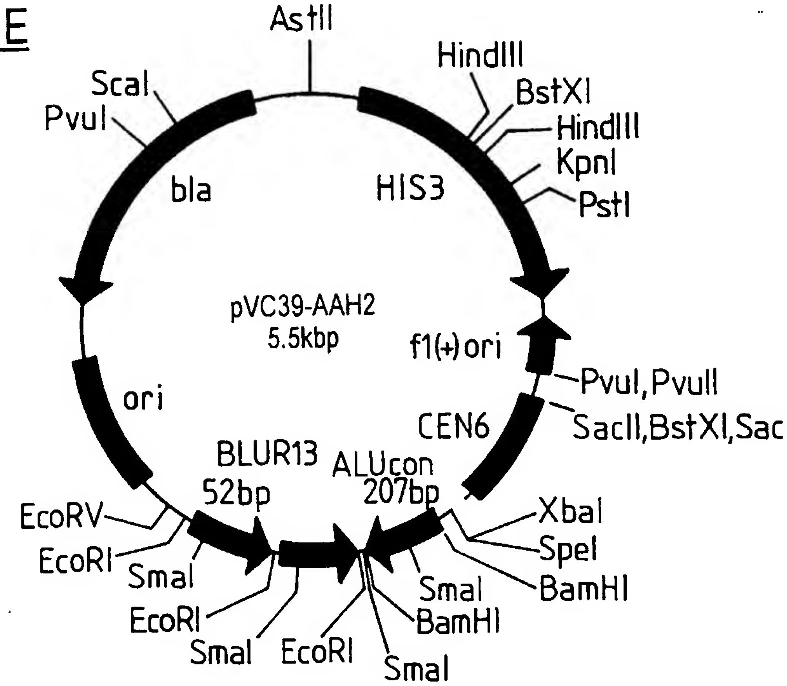

AstII
HindIII
BstXI
HindIII
KpnI
PstI
ScaI
PvuI
bla
HIS3
pVC39-AAH2
5.5kbp
f1(+)ori
PvuI,PvuII
SacII,BstXI,SacI
ori
CEN6
BLUR13
52bp
ALUcon
207bp
XbaI
SpeI
BamHI
EcoRV
EcoRI
SmaI
EcoRI
SmaI
EcoRI
SmaI
BamHI
SmaI

FIG 8 F

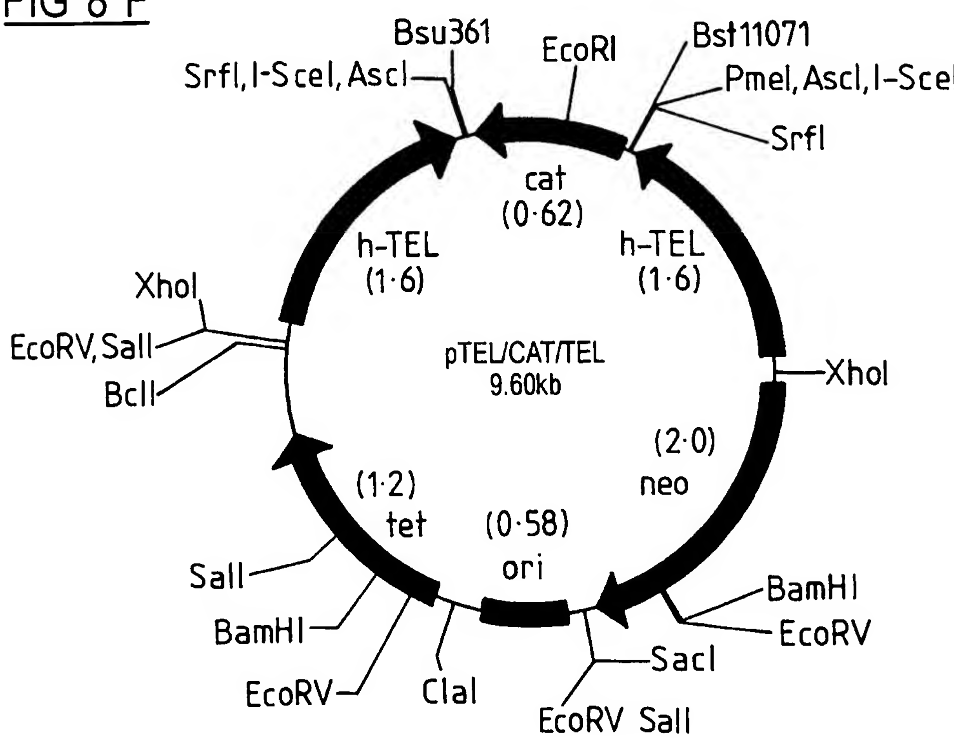

Bsu361
SrfI,I-SceI,AscI
EcoRI
Bst11071
PmeI,AscI,I-SceI
SrfI
cat
(0·62)
h-TEL
(1·6)
h-TEL
(1·6)
XhoI
EcoRV,SalI
BclI
pTEL/CAT/TEL
9.60kb
XhoI
(2·0)
neo
(1·2)
tet
(0·58)
ori
SalI
BamHI
EcoRV
ClaI
EcoRV SalI
SacI
BamHI
EcoRV

FIG 8 G

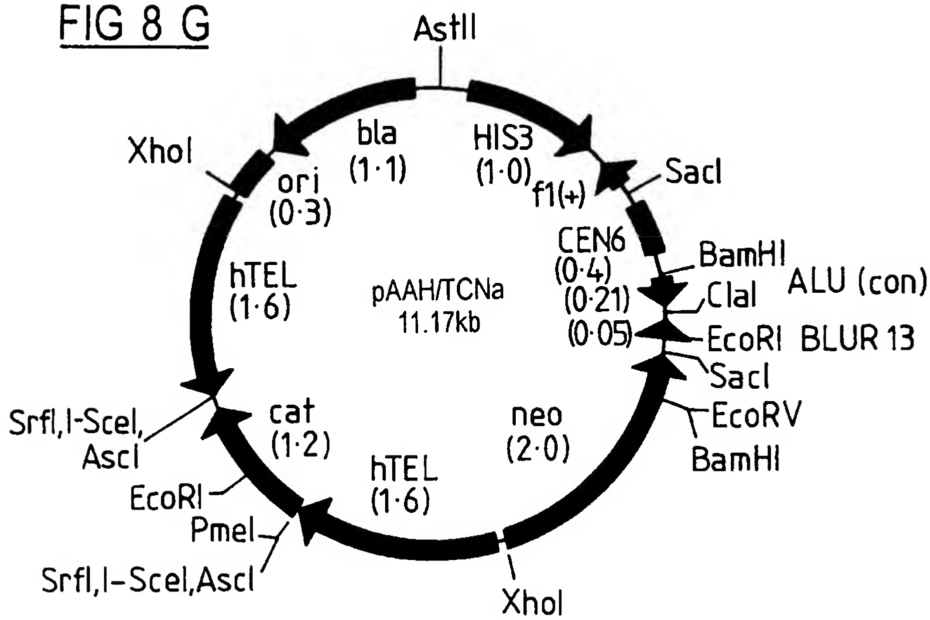

AstII
bla
(1·1)
HIS3
(1·0)
f1(+)
SacI
XhoI
ori
(0·3)
CEN6
(0·4)
BamHI
hTEL
(1·6)
pAAH/TCNa
11.17kb
(0·21)
ClaI
ALU (con)
(0·05)
EcoRI
BLUR 13
SacI
EcoRV
BamHI
SrfI,I-SceI,
AscI
cat
(1·2)
neo
(2·0)
hTEL
(1·6)
EcoRI
PmeI
SrfI,I-SceI,AscI
XhoI

FIG 8 H

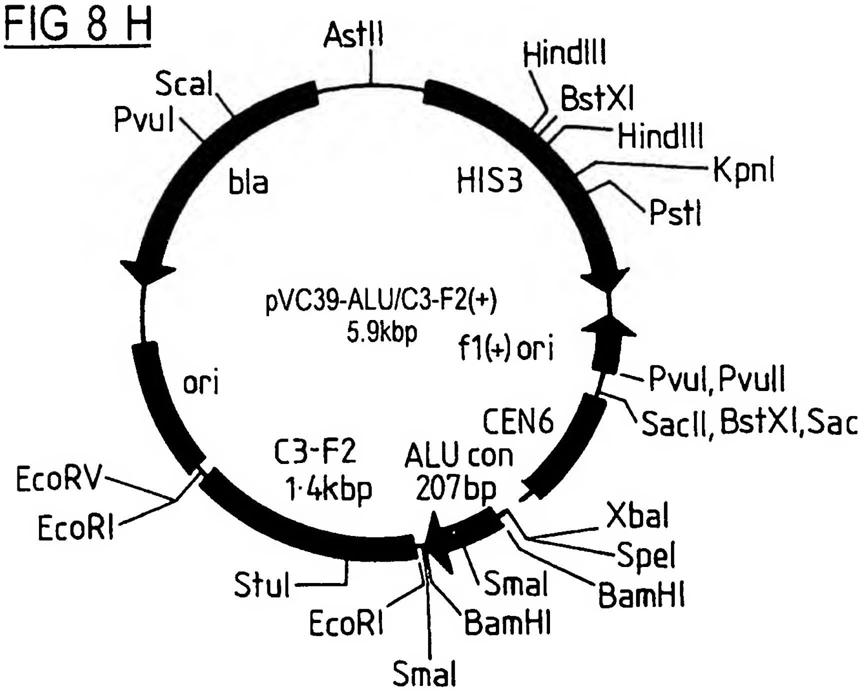

AstII
HindIII
BstXI
HindIII
KpnI
PstI
ScaI
PvuI
bla
HIS3
pVC39-ALU/C3-F2(+)
5.9kbp
f1(+) ori
PvuI, PvuII
ori
CEN6
SacII, BstXI, SacI
C3-F2
1·4kbp
ALU con
207bp
EcoRV
EcoRI
XbaI
SpeI
BamHI
StuI
SmaI
EcoRI
BamHI
SmaI

FIG 8 I

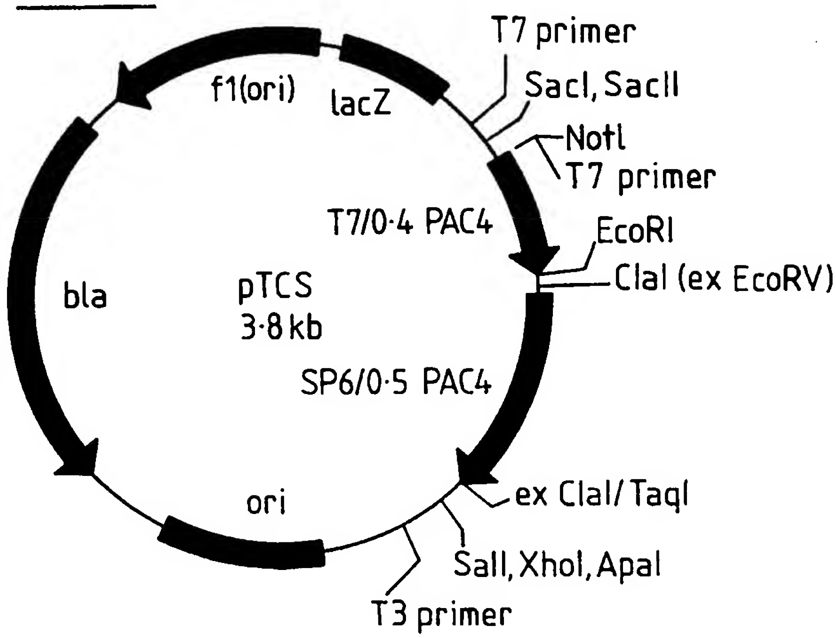

T7 primer
SacI, SacII
NotI
T7 primer
EcoRI
ClaI (ex EcoRV)
ex ClaI/TaqI
SalI, XhoI, ApaI
T3 primer
f1(ori)
lacZ
T7/0·4 PAC4
bla
pTCS
3·8 kb
SP6/0·5 PAC4
ori

FIG 8 J

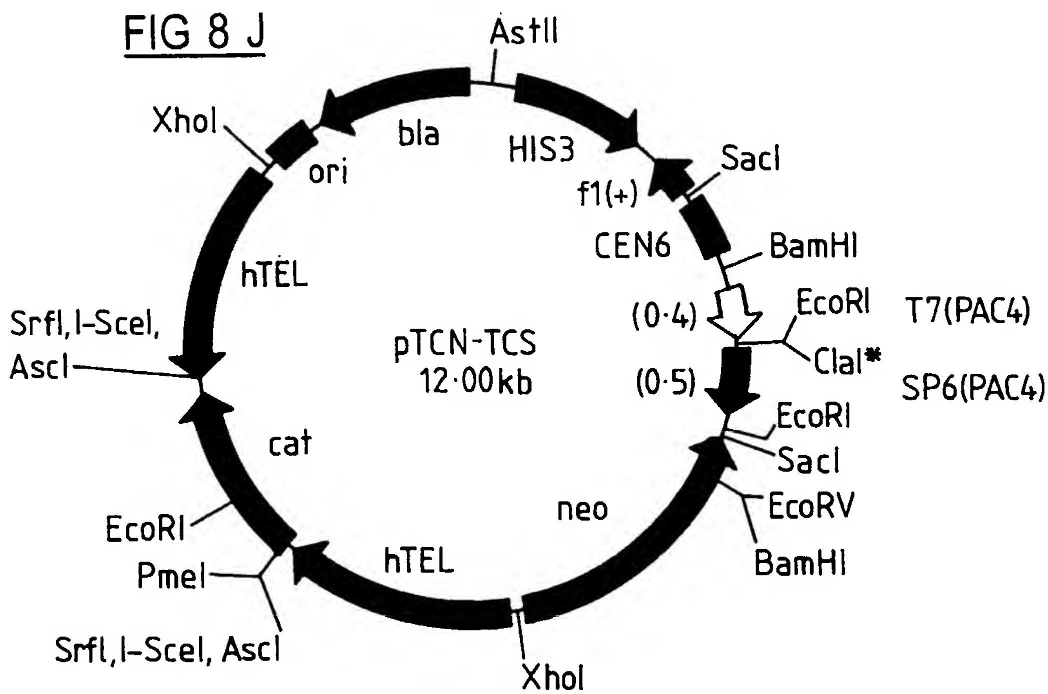

AstII
XhoI
bla
HIS3
SacI
ori
f1(+)
CEN6
BamHI
hTEL
(0·4)
EcoRI
T7(PAC4)
SrfI, I-SceI,
AscI
pTCN-TCS
12·00 kb
ClaI*
(0·5)
SP6(PAC4)
EcoRI
cat
SacI
EcoRV
neo
EcoRI
BamHI
PmeI
hTEL
SrfI, I-SceI, AscI
XhoI

FIG 9

Circular TAR

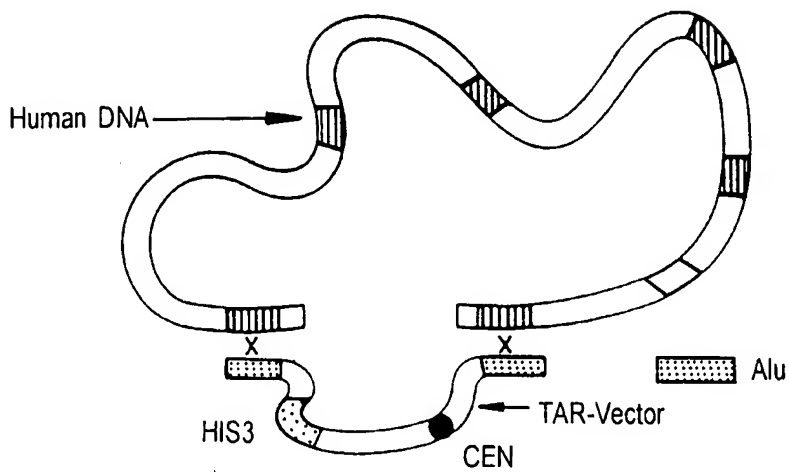
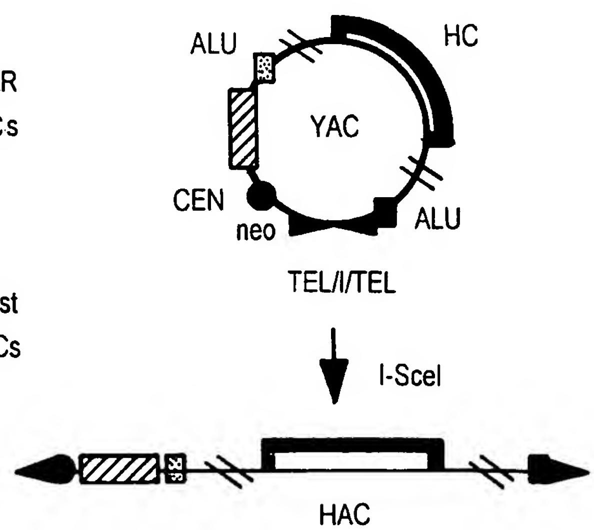


FIG10

Shuttle YAC to HAC

1. Circular TAR to create YACs

2. I-SceI digest to create HACs



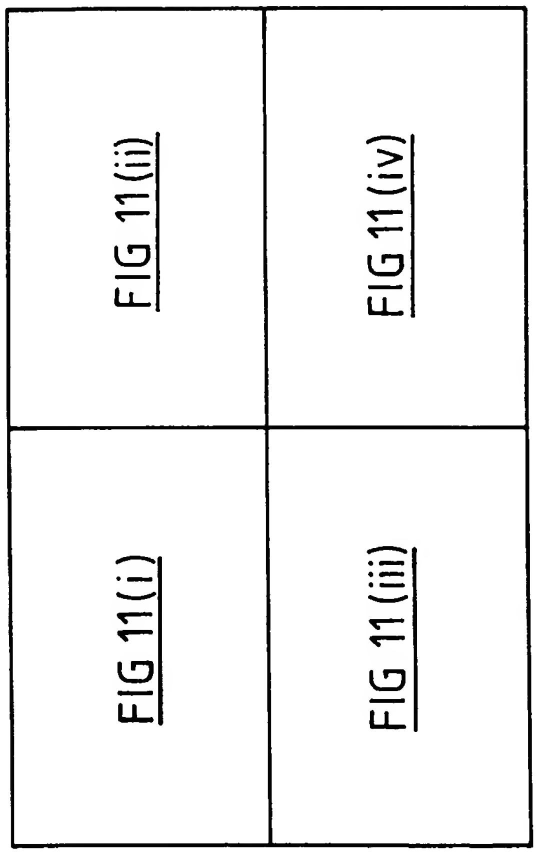


FIG 11

FIG 11 (i)

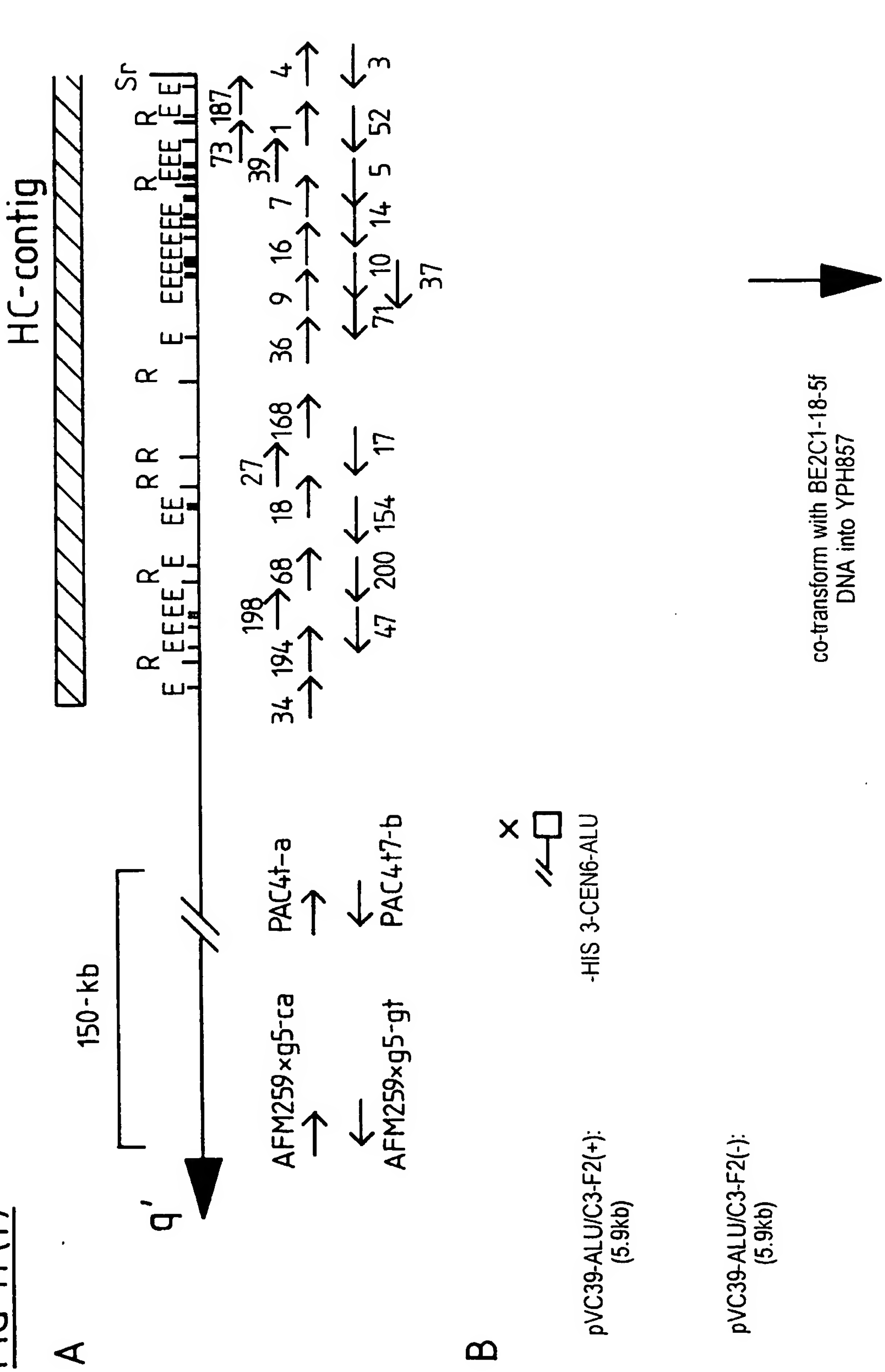
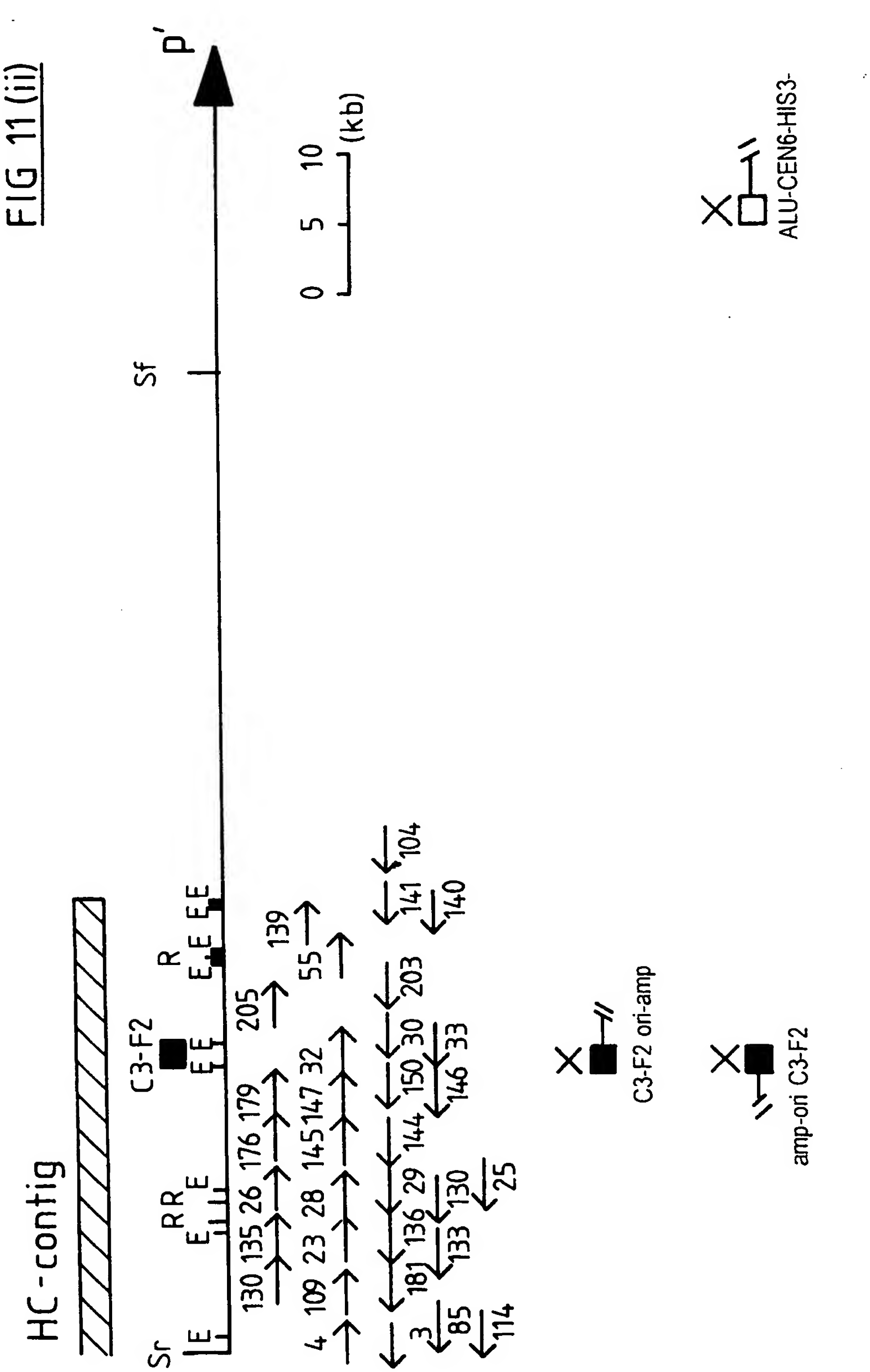

A
B
HC-contig
150-kb
q'
Sr
AFM259xg5-ca
AFM259xg5-gt
PAC4t-a
PAC4t7-b
34
194
198
68
200
47
18
154
27
168
17
36
9
16
7
39
1
73
187
4
3
52
5
14
10
37
71
-HIS 3-CEN6-ALU
pVC39-ALU/C3-F2(+): (5.9kb)
pVC39-ALU/C3-F2(-): (5.9kb)
co-transform with BE2C1-18-5f DNA into YPH857

FIG 11 (ii)


HC-contig
p'
Sf
Sr
C3-F2
0 5 10 (kb)
C3-F2 ori-amp
amp-ori C3-F2
ALU-CEN6-HIS3-

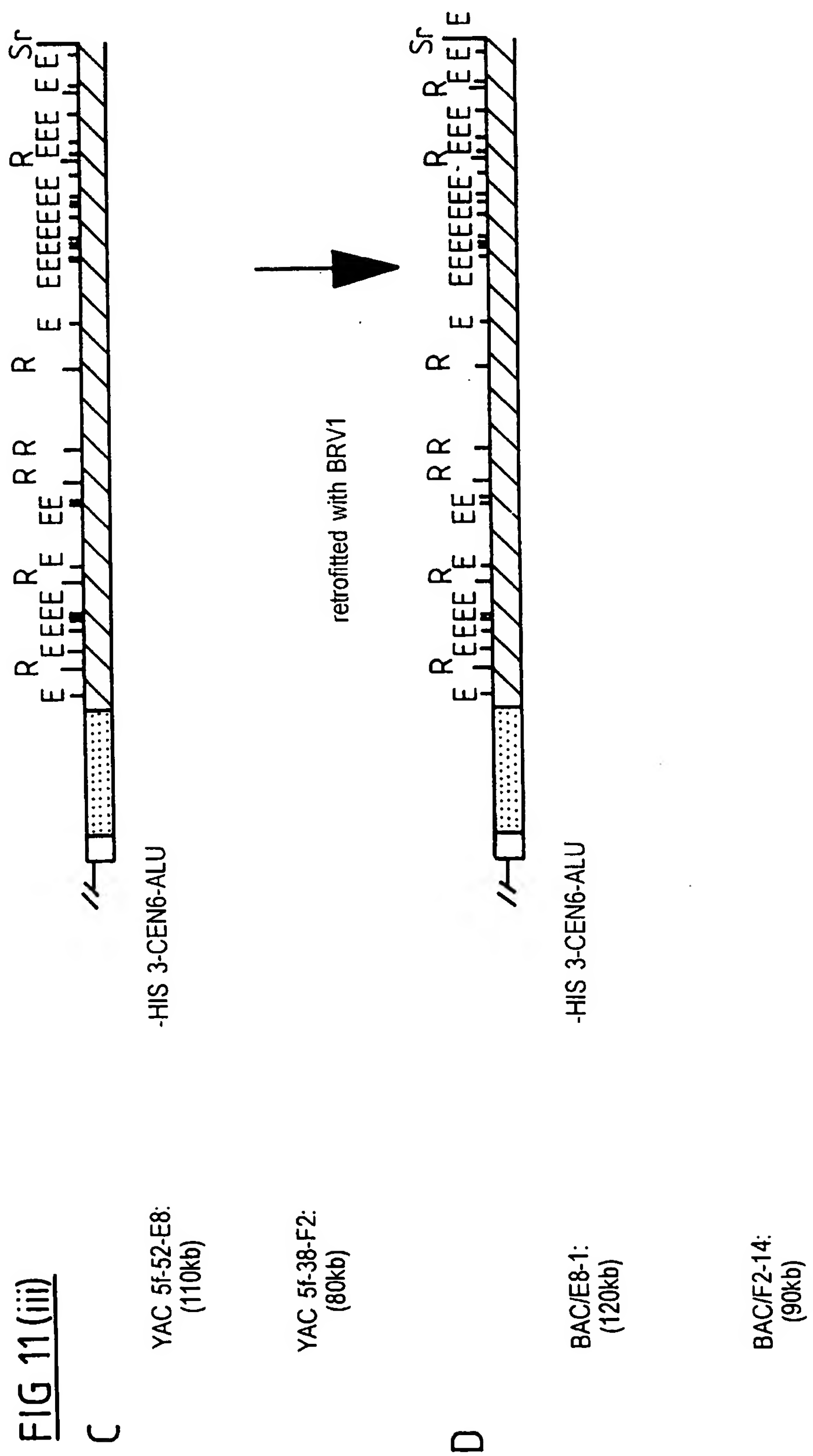
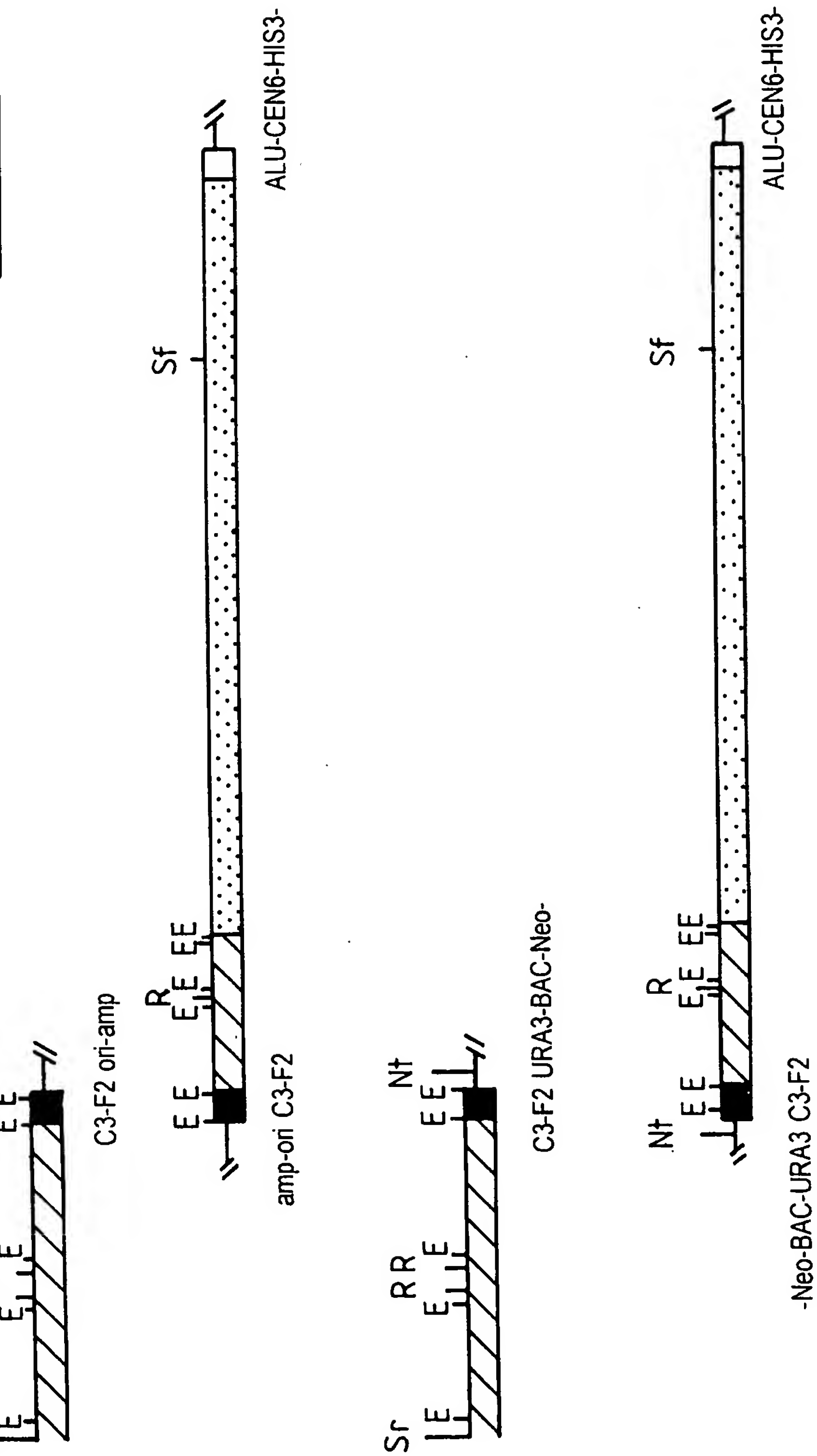
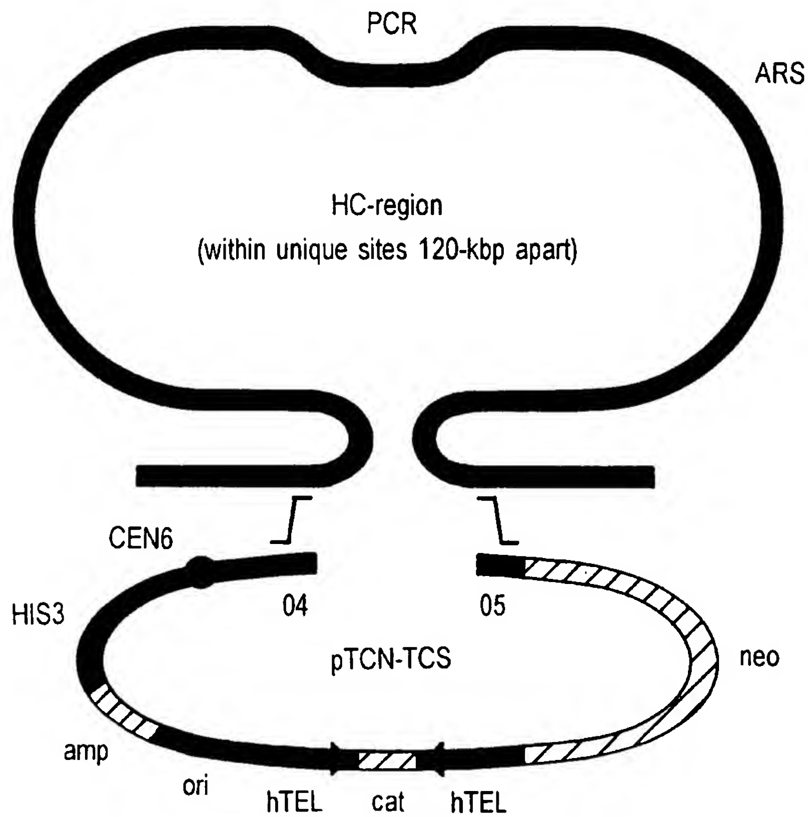

C
YAC 5f-52-E8: (110kb)
YAC 5f-38-F2: (80kb)
-HIS 3-CEN6-ALU
E R E E E E R E E E R R R E E E E E E E E E R E E E E E Sr
retrofitted with BRV1
D
BAC/E8-1: (120kb)
BAC/F2-14: (90kb)
-HIS 3-CEN6-ALU
E R E E E E R E E E R R R E E E E E E E E E R E E E R E E E Sr

FIG 11 (iii)

FIG 11 (iv)


ALU-CEN6-HIS3-
C3-F2 ori-amp
amp-ori C3-F2
C3-F2 URA3-BAC-Neo-
-Neo-BAC-URA3 C3-F2
Sf
Sr
Nt
R
E

Specific TAR of HC-region from mar (del) 10



1. Co-Transformation into YPH857
2. Select for HIS^+ colonies
3. Screen for HC-region by PCR
4. Prepare high-MW DNA
5. Digest with I-SceI to expose hTELs
6. Transfect HT1080 cells
7. Select for $G418^R$
8. Analyze by PFGE and FISH

FIG 12

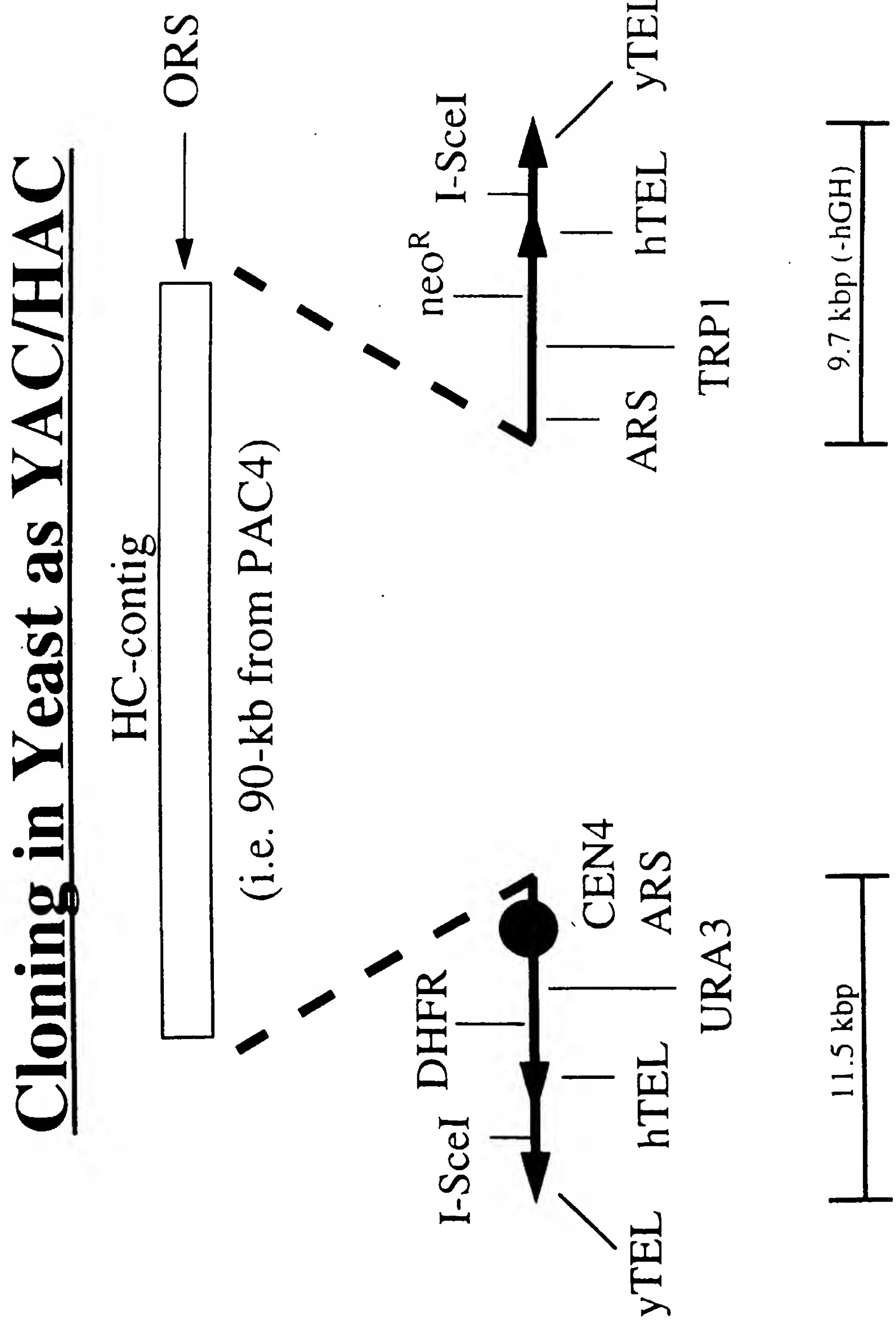
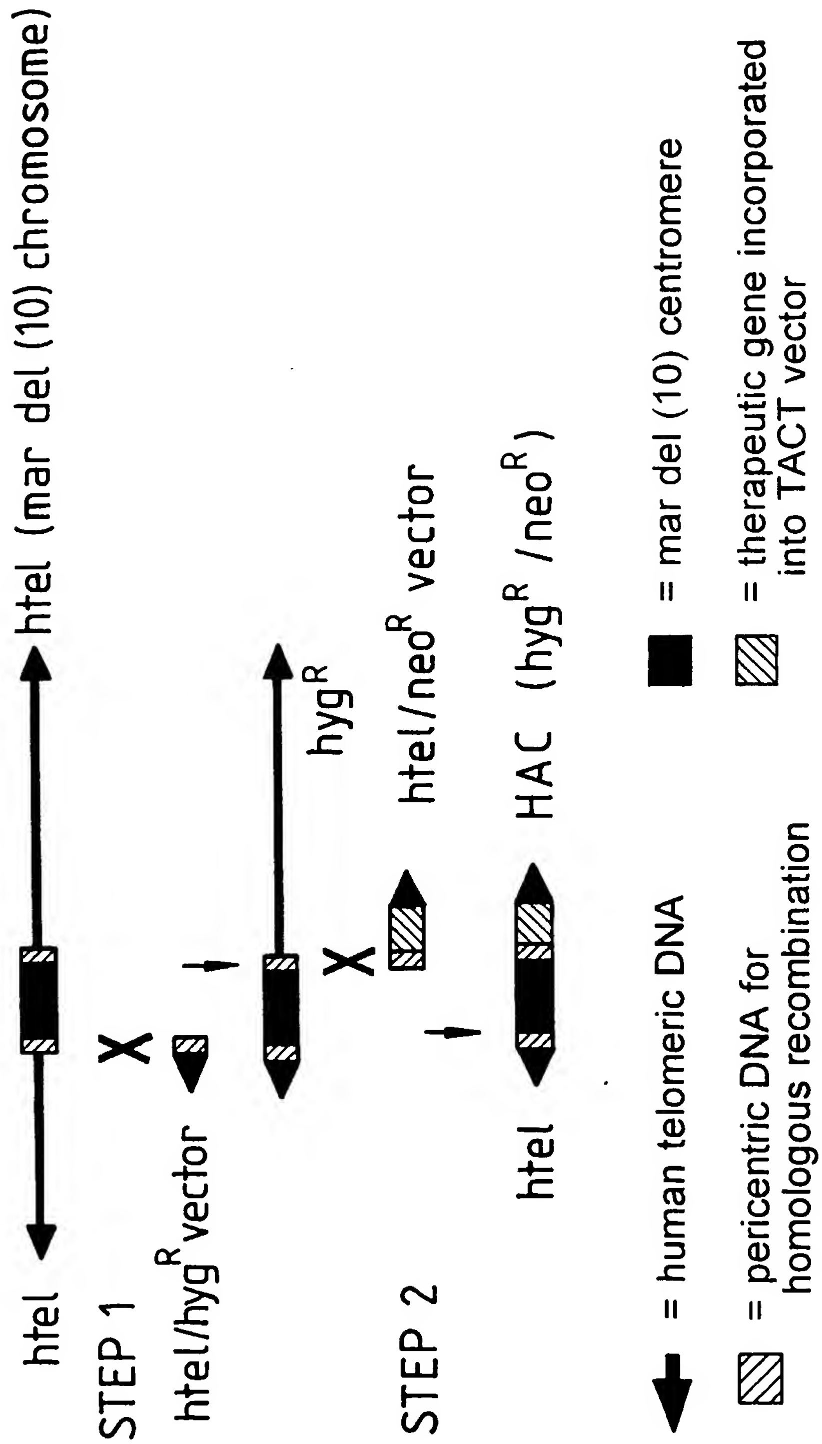

Cloning in Yeast as YAC/HAC
ORS
HC-contig
(i.e. 90-kb from PAC4)
yTEL
I-SceI
hTEL
DHFR
URA3
ARS
CEN4
11.5 kbp
neo^R
I-SceI
hTEL
yTEL
TRP1
ARS
9.7 kbp (-hGH)

FIG 13

FIG 14

Outline of TACT procedure



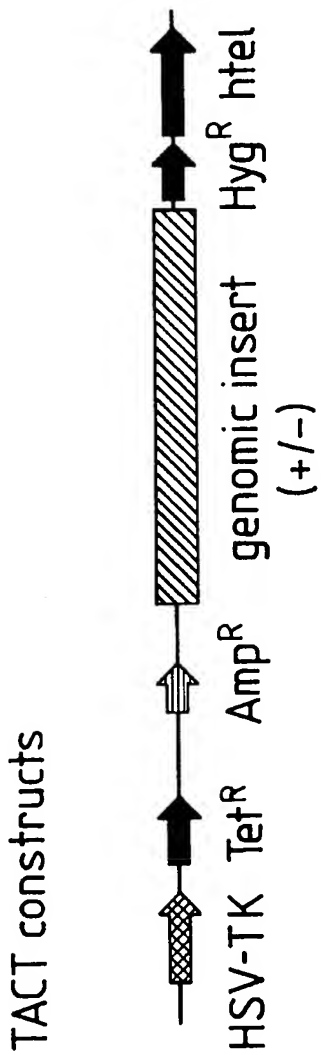


FIG 15A

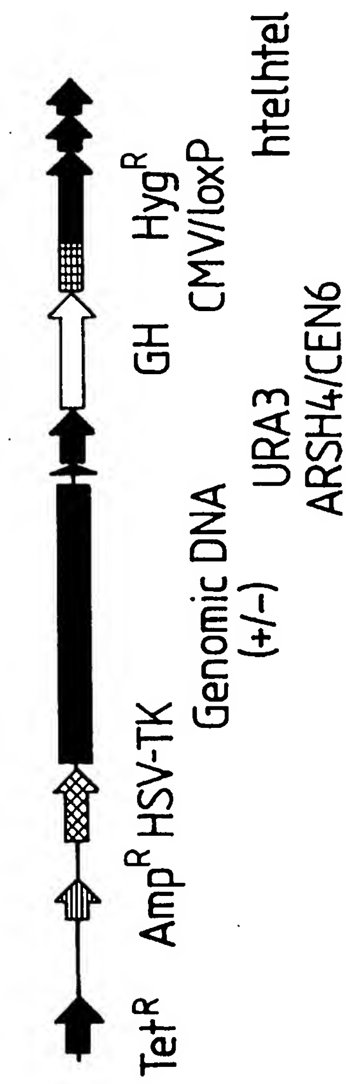


FIG 15B

159/285	170/285
160/285	171/285
161/285	172/285
162/285	173/285
163/285	174/285
164/285	175/285
165/285	176/285
166/285	177/285
167/285	178/285
168/285	179/285
169/285	180/285

FIGURE 16 (1)

TGGTTGATTT GTNNATAAGG AAGTTTGGAA TCAATCCCGG AAGGAATTTT TTTTTTAAAA

AATTTTTTGG AAGGGTTTGG TAWTAAAAAA RCCAATTTGG GTTTTTAAAA ATAGGAATTT

TATGGGAAAA AATTTTCCCT TTTTTTTTTT TTAAGTTTTA GATGTTATGT TTCCTTATAC

TTAAAGTGGG TGTCTTATAG GCAGCATATA TCTGGGTCTT GATGTATTAT TTAATCTGAT

AATCTCAACC TTTTTGTTGG AGTGTTTAGG CCATTTACAT TTAGTGTAAT TATAGACATG

GTTTGATTTG CTATACCATC TTTTCATTTG TTTTATATGT GAGCCATCTT TTCATTGTTC

TTTTTTCATC TTTGACCATT TTCTTTAGTA CTGAATACTT TTTTTGTATT TCATTATATC

TATTGGCTTT TTAGTTATAC CTCTTAAAAT TTTTTTTTCT GTTTTATGTA GGATTTATAA

TATACATCTT TAACTTATCA CAGATTACCT TCAAATAGTA TTTTACCAGC TCAAGTGTAA

TGTAGAAACC TTACAAGAGT ATATTTTCAT TTCTGTCTCC TAATTTTTAT GCTATTGTCT

ATAATACATT AGGTTTGTTG TTGTTTGTTT TTACCTTATT GCTGTTGGCT GGGGTCAGCA

FIGURE 16 (2)

AACATTTTCT GTAAAGGGCT AGATAGTACA GGCATACCTT GGAGATACTG TGGGTTTGGT

TCCATACCAC CACAATAATA CAAATATGCA AGAAGTGGAT ATCACAATAA AGTGAGTCAC

ACAAGTCTTT TGGCTTCCCA GTGCATATAA AAGTTTTGCT TATACTACAC TGTAGTCTGT

TCAGTGTGCA ATAGTGTTAT GTCTAAAAAA ACACATACCT TAATTTTAAA ATGCTTTATT

ACTAAAAAAT GCTAACAATC ATTTGAGCAT TCAGTGAGTT GTAATCTTTT TGCTGGTGGA

AGGTCTTTTC TTATTGATGA CTGATCGGGG GTCAGGTGCT GAAGCTTAGG GTGGCTGTGG

CAGTTTCTTA AAACAACAGT GAAGATTGCA ATATCAGTTG ACTCTTCCTT TCATGAAAGA

TTTCTCTCTA GTGTGTGATG CTTTTTGATA GCATTTTATG CACAGTAGAA CTTCTTTGAA

AATTGGAGTC AATCCTCTCA AACCCTGCTC TGCTTTAACA ACCTAAGTTA ATATAATATT

CTGAATCCAT TGTTGTCATT TCAACAATTT TCACAGTGTC TTCACCAGGA GTAGATTCCA

TCTCATTTCC TGAGATGGAA TCTTTGCTCA TCCATAAGAA GAAATTCCTC ATCTGTTCAA

FIGURE 16 (3)

GTTTTATCAT GAGATTGCAG CAATACAGTC ATGTCTTCAG GCCTCACTTC ACTTTTAATT

CCAGTTCTCT TGCTGTTTCT ACCACATCTG TGGTTCCTTC CTCCATTGAA GTCTTGAACC

TCTCCAAGTC ATCCATGAGG GCTGGAATCG ACTTCTTCCA AATTCCTGTT AATATTTATA

TTTTGACCTC CCATGAATCA TGAATGTTCT TAATGGCACC TGGAATGGTG AATCCTTTCC

AAAAGGTTTT CAATTTACTT AGTCCAGATC CATCCATCCA GAGGATCCAC TTTCAATGCC

AGTTATAGCC TTATGGAATG TATTTCTTCA ATAATAAGGC TTGAAAGTTG AAATTACTCC

TTGATCCATT TTCTGCAAAA TAGATGTTGT GTTAGCAGGC ATGAAAGCAA CATTAATCTT

TTTGTACATG TCCATCAGAG CTCTTGGGTG ACCAGGTATA TTGCCAGTGA GCAGTAATAC

TTTGAAAGGA ATTATTTTTC TTAGCAGTAG GTCTCAACAA TGGGCTTAAA ATATTTGGTC

CACCATTCTG TAAACTGATG TGCTGTCATC TAAACTTTGT AGTTTCATTT ATAGAGCACA

GGCAGAGTAG ATGTAGCATA ATTCTTAAGG GACTTAGGAT TTTCAGAATG GTAAATGAAC

FIGURE 16 (4)

ATTGGCATCA ATTTAAATCA CTAGCTGTAT TAGCCCCCAA CAAGAGAGTC AGCCTATTTT

TTGAAGCTTT GAAGCCAAGC GTCGACTTCT CCTCCCTGGT TACAAAAGTC CTAAATGGCA

TCTTCTTCCA ATATAAGGCT GTTTTATCTA CATTGAAAAT CTGTTGTTTA GTGTAGCCAC

CTTCATCAAT GATACTATCT AAATCTCTTG GATAACTTGT GCAGCTTCTA CATCAGCATT

TGCTACTTCA CCTTGTACTC TTATGTAATG GAGTGGCATC TTTCCTCGTA CCTCATGAAC

CAACCTCTGC TAGCTTCCAA CTTTTCTTCT GTAGTTTCCT CGCCTCTCTC AGCCTTCATA

GACTTGAGGA TAGTTAGAGA CTTGCTTTGG ATTAGATTTT GGCTTCAGGA AATGTTGTGG

CTGGTTTGAT CTTCTATCCA GACCACTAAA ACTTTATCCA TATCAGCAAT AAGGCTGTTT

TGCTTTCTTA TTATTTGTGT GTTCACTGGA GTAGCACTTT TAATTTGCTT CAAGATATAT

TTCTTTGCAT TCACAACTTG GCTGACTGGT GCAAGAGGCC TAGCTTTCAG ACTATCTTGG

CTTTTGACAT GCCTTCCTCA CTAAGCTTAA TCATTTCTAG CTTTTGATTT AAAATGAGAG

FIGURE 16 (5)

ATGTAGGCCA GGCACAGTGG CAGGCACAGT GGCATATGCC TGTAATTCCA ACACATTAAG

AGGCCAAGGT GGGAGGATTG CTTGAACCCA GGAGGTGGAG GTTGTAGAGA TCACACCACT

GCATTCCGTC CTGGATGACA GAGCAAGACC CTTTCTCAAA ATAAAATGAG AGGTGTGCTT

CTTCTTTTTG TTTGAGCCCA TAGAAGCCAT AGTATGATTT TTAATTGGCC TAATTTCAAT

ACTGTTGTGT CTCAGAGAAT AGGGAGGTCT GAAGAGAGGG AGAGAGGTGG GGGAATGGCT

GGTCAGTGGA GCAGTCAGAA CACACATAAC ACTAATAAAT TGTTTGCTGT CTTATATGGA

TGTGGTTTGT GATGCCCCCA AACAATTACA ATAGTTACAG CAAATATCAC TGATCACAGA

TCACCATAAC AGATATAAGA ATCATGGAAA AGTTTGAAAT ATTTTGAGAA TTAGCAAAGT

GTGACACAGA GAAACAAAGT GAGCACATGC TGTTGGAAAA AATTGGTGTT GATAGACTTG

CTCCATGTAA GTTTGCCATA CGCCTTCAAT TTATAAAAAA CACAATATCT AGGAAGTTCA

ATAAAGTGAA GTGCAATAAG ATGAAGTATG CCTGTAAATA TTTCAGGCTT TCCAGACCAT

FIGURE 16 (6)

AGGGTTTCTG TTGCAACTGC TCACCTCTGC CATTATAGCA TGAAAGCAGC TATAGAAAAT

ATACATAAAT GAGGCCTGTA ATCCCAACAC TTTGGGAGCC CAAGGTGGAT GGATCACTTG

AGGTCAGGAA TTCGAGACCA GCTTGGCCAA CATGGCAAAA CCCCGTCTCT ACTAAAAATA

CAAAAATGAG CCAGGACTAC GCATGCCTGT AGTCCCAGCT ACTTGGGAGG CTGAGGCAGG

AGAATCTCTT GAACCCGGGA AGGGGAGGTT ACAGTGAGCC AAGATTGTGC CACTGCACTC

CAGCCTGGGC AACAGAGTGA GACTGTCTCA CAAAAAAAAA AAAAGGAAAA GAAAATACAC

ATAAATGAAT GTATGTGGCT GTGTACCAGT ATATCCTCAT GCTCTAGCTT GCCAACCCTT

GCTTTACACT GTCAGTTACC TTCTAAAGAG ATTAAAAATC ATAACAATAT CTATTACGTT

TATTCACATC CTAGTGTCAT TTCTTCCTTA TGTAGAATCA AATTTCATTC TGGTATCATA

TTTCTTCTTT CTAAATAATT TCCTTTAATA TTTTTTATAG CACAGGTCTA ATAGCAATGC

ATTATGCAAT TCATTGCTAT TAGACCTGTG CTATAAAATA GCAATGAATT ATGTCAGTTT

FIGURE 16 (7)

```
TTATTTGTCT GAAAAAGTTT TTTGTTTTTG AAATATACTT TTGCTGGGTA TATAAATCCA
TGTTGCATAA CTTCTCTTTT CTTCAGCACT TTAATGAAGT CACTCAGTTA TCTTCTGGCT
TGTATAGTTT CTCTGGCTGC CTTCAAGATT TTTTCATTGT CTTTAATTTT TAGCAGTTTG
ATGTGTCTAG GAGTGATTTT CTTTGTATTT ATCCTTTTGG GGGCCTCTTA ATTTCTTTGA
TCCTTTTTTT CTTTTTTTTT TTTTTTAAAC CATTTTGGGT CTTTCCCCCC ATTTGGGGTG
AAAAAAAAAA AAAAATAAAA TCATAGTTTA AAAAACTAAT TTTGGAAAAT TTTCAGCTAT
CATTTCTTCA AATATTTATC CTACTCTATG CTCCCCTCCT CCCCTTTCCT TCTGTGACTC
AAATTACAGG TATATTTAAC CATTTTATTT GTTCACGGCA CTTGGATGCT CTGCTTTCTT
ATTTTTTGTC TTTCATTTTG GATAATTTCT ACTGACCTAT CTTCAAGTTC ACTGATTCTT
TTCTCAGTCA TGTCTAGTGT GCTCAACGCC TGTTGAAGAA ATCCTTTGTC TTTAATATCA
TGTTTTTTAT TTCTAGCATT TTCATGTAAC TCTTTGTTCT GGTTTCCATC TCTCTACTCA
```

FIGURE 16 (8)

CTTTTTTTTT TTTTTTTTTT TTTTTTTTTT TTTTTTTAGA CAGAGTCTCG CTCTGTCACC

CAGGCTGGAG TGTAGTGGCG CGATCTCGGC TCACTGCAAC TTCCGTCCCC TGGGTTCAAG

TGATTCTCCT GCCTCATCCT CCCGAATAGT TGGAATTACA GGTGCCCACC ACCGTGGCTG

GCTAATTTTT GTATTTTTTT AGTGGAAACA GGGTTTCACC ATGTTGGCCA GGCTGGTCTT

GAATTCCTGA CCTCAGGTGA TCCACCTGCC TCAGCCTCCC CAATTGCTGA AATTACTGGC

ATGAGGCACT GCACCCAGCT CTGCTGACAT TTTTTATCTT TTGCTGCATT TTGTCTACCT

TTTCCATGAA ATCCTTTAAC ATAGTAGTCA TAATTACTTT CAATTCCTTG TCTGACAGTT

CTGACATTCA AGTCTAGGTC TGTTAATACT TTGTGAATCT GTTAACAGCT TTTTTTCATT

CTTGTCTGTG TGTTTTGTAT TTCTTGATTG TATGCCAAAT ATTGCCTGTA AAATAAACTT

AGATAAGTCA TACTTCTATC CAGAAATAGC ACATTTTTTG TGTCCAGTCA TTATGTGGAG

GAGTTGGGGC AGTCTATCAG TGGCTGAACT AGTTTGGATT TGTTGATGCT ATACTTAGAA

FIGURE 16 (9)

TGCACCAGAC TTCCATTCAC TGCAAGAGTG GGCTGCTGCG CTTTGTGATT CATGTGAGGC

CTGAATTGTG GAAGGGTTTT TCCTTAGTGT GTCCCTCCAT GCTCAGATTT CAGCAAGTCT

TCATATCTGT GCCACAGAAG GAATCTGACC CATGCTCTTT TTGACCTCCC CAAGTGATCA

ACTGTTGCTT GTTATAGCTT GTCATGGAGT AAGAGGGTGT TTTTTTAGTT TTCATCCTCC

AGCCTTGGTC TTGGGCCCTG AGCTCCTAGA CTCCAGGAGT GGATGGAATC CAGTGATTTC

TCAGTAATTC AGCCCCTTCT CCAGTAGTGG CAGATCTCTG CTTTGTATCA GTGCAAGATC

CTGGGCTGAG CTCATTTTCT GCCCTTCCTC GAGTGGCAGA CAGCTCTTGC TTTCACCCTT

CTACCAAAGG CAGTGCATCT TTTCTTGGGC CTCTCCCCAT TGAACTTATG ACTTTCACAT

AAGAGAAGGG CTCATGTATC AGAGAATTCT GTGACTTTGT GCCACATACA GAGTCTCTCA

GTTCTCTTGC CCTGCCCCAG TCTTTTTTGT GAGCACCTAG TAGAGACCCT TGGAGAAGAG

CAAGGAAGCG AGTATGGACT TCTTTTGTGT CTGTCGATTG CTTTGTTTCT CAACTGCTAC

FIGURE 16 (10)

TCTTGGACTT TAAGAATTCA TTAAAATTTC AGCTGTTTTC TTTTTTTCTT TCGTTTTTCT

TTTTTTTTTT TTTTTTTTTT AGATGGAGTC TTGCTCTGTT GCCCAGGCTG GAGTGCAGTG

GTGTGATCTT GGCTTGCTGC AACCTCCGCC TCCCGGGTTC AAGCGATTCT CCTGCCTCAG

CCTCCCAAGT AGTTGGGATT ACAGGTGCCC ACCACCACAC CTGGCTAATT TTTGTATTTT

TAGTAGACAC AGGGTTTCAC CATTTTGGTC AGGCTTGTCT CAAACTCCTG ACCTCATGAT

CTGCCCGCCT CAGCCTCCCA AAGTGCTGGG ATTACAGGCA TGAGCCACCG CGCCAGGCCT

CAGCTGTTCT CTTTTTACCT GCTGGGATGG CTAGTTTTCT GTGTCAACTT GACTGGGCCA

TGGGATGTCC AGATATGTAA TTAAACAGTA TTTCTGGGTG TTTCTGTGAG GGTGTCTTCA

GAAGAGATTT GCATTTGAAT TGGTGAACTA AGTAAAGCAG AGGGCCCTGT CTAGTAGGGG

TAGGCATCAT CCAGTCTGTT GAGGACTTGA ATAGAACAAA AGGCAGGGGA AGGTTGGAAT

TGCCCCCTCT CTGCTTGAGC TGAGACATCT ATCCTGCCCT TGGCACTCCT GGTTCTCAGG

FIGURE 16 (11)

GGTTCAGACC TGGATTCCTG GTCTCCACCT TGCCCATGGC AGACTGTGGG ACTTCTCAGC

CTCCTATCTA ATTAATAAAT TTTTTTTTAC ACACACACAC ACACACACAC ACACACACAC

ACACACACAC ACACACCCTA TGTATCCTTC TGTTTTTCTG CAGAACCATA TTTAATACAC

CTGCTTTTAT GACGATTACC TATCGATTCT GTATTCTGCC AAAACTGAAA ACAGTTCATT

TTTCCATCTC TTCTCAGAGA GGCTTGTCAG CCATTAGTTC TCTGATGGGC TCAAGAAGTT

ATGCAGTTTT TTTTTTCTCA CTGTTAGGAT GGAATTGATA TTCTGTTGAA ACTTTCTATA

CCTAAGTGGA AACTTGTTTT GAGGTTATTT TCTCTACTTA CTTTTGCTGG AAATGGAACA

CTCTGTATCT AGTTAAGACA CATAAACTGA CTTGTGATAC CATAATGTTG TGTTGAATTT

TATATTCTTA GAAAATCATC TGTCAAGGTG TTAACTAATG GCAAAGCATT TAATAAATCA

GCATTCATGT ATTCAGGTGC TCTGAATTAT CTGACTTTTA AATTCTTACT TTATAAATGA

GAAAATTGGG GCATGGAAAA GTTAACTCTC CTAACCCCGA ATTATTACAT TATTAAGGAC

FIGURE 16 (12)

AGGACTTAGA GGCCAGATAT CTTAAGTCAT TAATATTCTT TGGCTCACAG AATTGGCAGT

ATAACCTAAA GGTAATAACT AGGTGATTTT CTTTTATATC AATTAAATAT GTCAGTTTTC

AAATATTCAT AAGTACCTAC TGTGCAGGGA AAGAACATGC CATACAAAAG ATGTAGTCCA

GGCCTTTAAG AAACTTTCAT TTAATGGGAA CTCAAGAAGT GTACATATAA GGAGGGAAGT

AGCAGTATGG TACAAGATAA TACATACATA TCAGTGAATG ATATTGCCAA AAAGTGCTAT

TGATAGAGCA ATAATTCATT TCTGCAAACA GCTGCTGATC TCCTACTGAA AACAGAGGAG

GGAGAACAGG ACGCCTCGTG GTCAGGATAG AAGAGAAAGA CCTTGAGTTG AGCCTTGAAC

AGTATTTAAT ATTCAAAAGG TTAAGAGAGG AGAGCAATTG AGGAGGGGAG AATAGTTCCA

GCACAAATGA TGGTGTACAA GATGAACACA GTCAGTAAAG AGCAGACTGG TCTGGATGGA

GAGGAGGATT TGCATCATTT GGGATTACGT CATTTAGACC CTTGAAAGCC AGGATTGAGT

AAAGCCACAG TGAAGCGACT GGCTCGTATG GAAGCTTTAT TTTAAGAAGA TTAATCTGGT

FIGURE 16 (13)

AGTGACATGT GCCAAAAACT GAATAGGTAG AAATGAGATG CAGAGAGCCC AGTTAGAACT

AAGTCTGGTG CAGTAATGCA GGATTGAGGC AATAAACACC AAACTACAGT ATCACCAGAT

AATGGATGTT TGAACGGACG GTTTAAAGGA AAATTGATGG TATTTGGTAA TTTATTAGAT

AATCCAGGGC CATGGAATGA GAGGGGAAAA TGACTAACCA TAGTCATCAA ATGGTTTTTC

TTAATGAATC TGAATTTTGG TGTAAGAGCA ACATTTTCTT AGGCCTTGCC TAGTTGGTAC

AGCTGACTAT GATAATGACT GCTACCATGC TTGTTCCTCT TTTAGCAGCT GTGAGTCCCC

CACCAGCCAA ACAATGAGCC TCTTGAAAAG GACGATGCCT TTTCACTTCT CTCCAAGTGC

TTGGCAAATA GGAGGCCTTT TGAAGTTACT TTATAGTTAG GGGTTCCCAG TGAGTATTTG

AAATATTAAG TCATGCCCGT GGTTGACAGC ATGGCCCTAC TGCTCATCAT CAGCTATTAA

CCTTAGGCAA GTTAATGAAC TTTTCTAAGC CCCAGTCTAC TCATTTATAA AGTGGGATTA

TTAATAATGT CTACTTCATA AAATTATGAA GCCTGAGTTA GGTCATTCAG ATAGTGTTTA

FIGURE 16 (14)

GTCTGATTCT TCGAACCTAG TAAACAGTCA GTAAACAGAA GCAAATGCCA CATGCCTGAT

TTATATCCAA GGGGAGAAAG GTAAAAGTGA AATTTTCATG ATTTATGGAT TCAAATTATA

CATTTCAAAG ATGCTTTATA AGCTATTGTT TTGGTAAGAA GAATTGAGCT GAAACAGAAT

TTTCTGACAG CAGTGATTAT TAAATGGTGA AATAGGCTAT TGATGTCTTT AGAGGATATA

GATGTTCACC TTTTGCATAT AAGTGCACAA AAATTCACTA AGTAGATATG TCTGTCTACA

CAGAGAGAGA GAGCGTGAGA GCATTAAAGT TAGTAAACAT CCCCCTCGCT TTTTTTTTTT

TGAGACAGGG TCTTACTCTG TTGCCTAGGC TGGAGTGCAG TGGTGCAATC GTGGCTCACT

GCAGTCTCAA CATCCTGGGC TCAAGCGATC CTCTCGCTCA GCCTCCTGAG TAGCTGAGGT

GTGCACCACC ACACCCGGCT AATTTTTAAA TTTTTTTATT GTAAAGGTGA GGTTTCACCA

TGTTGCCCAG GTCTCAAACT CCTGAGCTCA AGCAATCTGC TCACTTCAGC CTCCAAAAAT

GCTGGGATTA CAGGCGTGAG CCACCACGCC TGGCCAGTAA ACCCCATTCA TTTACATCAT

FIGURE 16 (15)

CTTACTTGTC CCTCCAAAAT CCTGCAAAGT AGGTAGGTTC TGTCTTTATT TGTTATTTAG

GTGAAGAACT TGAAGTGGTG TTGAGGAATA GGTGTTTTGC CAAGAGTCAC GCAGCTGGAG

TGGCAGAGCT GTATACTCTT CTGATTCCAC CAACGCTGTT TACATCACAT CTGGAGAAAA

GTGCTCTGAG GCACAGATGT TTAGTGGGAG GGATGAGACA CAGGCTGCAA TGCCTAAAGA

TAATCGGGAA TAAAAGCAGA AAACAAGACG TTTGTTTCTG TTAAAATGAG ACAGAAAATA

AGGCGTTTGT TGTTTGGGAT TGAGCACTTG GAGAAGTGGG GAGCGATTTG ATTTGGGTGA

GACTGCTCCT GGAATGCTGC ATCTGGTTCT GGACTACTCA TTACTAGGCT TATAGAAACT

AGCTGGAGGA GGTTCAAAGA AAAGCTCCAA AATGATTAGC GGGCTGACGG GATTGATTTA

TAAGAAATAT TAAAAGAATT AAATGTGTAT AGCTCAGCTA AGCAAAGATG AAAGAGACCA

GCTAAATGTA TACAAATATC TGAAACGTGC AAACTTTAAA AAGAGAGATT AATTATTTAA

CATGATACAC GGGGGCACAA TATGCAGTCA CAGGATGAAA ATTTCAGCTG AGTATCTAGA

FIGURE 16 (16)

```
AGAATTCCCC GATAGTGAAT CTGTTAAGGC TGTCTGTAGT GTGGCCTTTC CCTGGAGAGG
CAATAGAAAT TTCAAGTCTT ACGATTTTAA AAGTTTCTTG GGAACTAGGT ATTAGATGAT
GTTAGAGAAT TATTATTAAT TTGGTCAGGT ATGATAATGG TATTGTAGTT CTATAAGAAA
AATTGTATTT TTTAGAGTTA CATACCCTGA AATATAAGCA TAGAATATGA TGTAGGAGAT
TTGCTTTAAA ATACCACAGT AAGGAAAGAA AGGAAGGAGG AAGAAAAGAA AGGAAGGGGA
AGAAAGGGAA AAAGAGGCAA AGAAGGAAGA GAAGGTAAGA GAAAGAAAAA GAATGAAGGA
AGAAGGCTGG GCACTGTGGC TCATGCCTAT AATCCCAGCA TTTAGGAGGC CAAGTTGGGA
GGATCACTTA ATTAAGCCCA GGAGTTCAAG GCTGCAGTGA GCTGTGATTG CGCCACTGCA
CTCCAGCCTG GGTGGCAGAG TGAAGCCCTG TCTCTAAAAA AAAAAAATAA GTTAAAAAGA
AAGAAAAGGA TAGATGAAGT ATGGCAAGAT GTTGGTAATG TTGAACCTGA AGGAAGTTAA
TATGTGAGTT CACTTTCCTC TTCAGTCTTC TTTATGTATG TTTGCCAACT TTCATAATAA
```

FIGURE 16 (17)

ACAATTTAAA TTATATTTTC CTGATCAAAA CTTAGTAGCA GTATTAATCC CTGGGCTTCC

TGACTAGAAC AGCCTCATTA CCACATGGGC AGAGTTCTGG CCGACCAGGG ACCACGTAGT

GGTTCACCAT CTTGCTCTGG TAATGTGGTC TGGGCTGAAG GGCCCTTTCT AAGGTTGTAG

ATAGAAATCC AGGAAACTTG TTAGAACTGC AGACCTATCA GGGTACCTGC AGGAGGTGAG

TCTACTAAGG TGAAAAAGCA GAGGGCAGAG GTCGTGATTA GCAGCTGACC GCCCCCTGCT

TTTCTGTCCC TCATTCGTGG AAAATTGAGT GGAGCTCAAT TTTGAGTGGA GCTCTAAGTA

GCTCCACTTG TAGACATTGA GTGGAGCTCT AAGTGTCTTC AGAATAGCAA AACACTAGTT

TTCTTTTTCT TTTCTTTTTT TTTTTTTGGG AGACAGAGTC TTGGTCTGTC CCCCAGGCTG

GAGTGCAATG GCACGATCTC CGCTCACTGA ACTCTGCCTC CCGGGTTCAA GCGACTCTCC

TGCCTCAGCC TCCCGAGTAG CTGGGATTAC AGGTGCCCAC CACCACGCCC AGCTAATTTT

CCTATTTTTA GTAGAGATGA GGTTTCACCG TGTTGGCCAG GCTGGTCTCA AACTCCTGGC

FIGURE 16 (18)

CTCAAGTGAT CCGCCTGCCT TGGCCTCCCA AAGTCCTGGG ATTACAGGTG TGAGCCACCA

CACCCAGCTG CAAAACCCTA TTTTTCTTGA ATGGAGAAAC ACTTTCCCCT TATTTATTGA

GTTTGGGAAG CAAGAAGAGG GGTAATTCAT TAAGTGAAAA TTTCCAAAAT CCAGAAAACA

TCGATAAAGC AGCAGCTTAA TTTTTTTAAG GAAGAATTTT TTAAACTATC TTCTTTTGAG

CCTCTTTAGG AAGACCTCAC GTCCTTGCCT TGAATGTTGA GAGTGGGAAA TCCAGGGAGG

TTTTGGAATG CATGCCTTAT GTCTGCTTTT TTGTTTGTTA GAGAAATATA AATATTTTAT

CTAGGTTTTG CTGATGGCAG TCAAGCATGA ACACAACCCA CTGTTTGAGA AGCTGTAATT

TCTGAATTTC TGCAGAGTGC ACATCTAGGC CAGCAAATGG CAGTAAGAGT GAGGTGGATT

TAGCTCAGTG TAAGGATGAA CTCCAGAACC ATCGGCTCTG ACTGAAAGTG AAGCGGCAGC

CGCGTTGTGG GAAAGCTGGC TGGAGTCTCT CTCATAAGCA GGCATTCTTT TTCTCCAGCC

CGTCACTGTG TTGGTTTGGG CCCACGGTAA GCCTCCTGGC CTCTAGGCTG TAACCCCCAC

FIGURE 16 (19)

CATCCTCCTC TGCCTCGCCT CCAGAGTGAT TGTTCTGAAG CACAACTGGA TGTCATTCCC

CTTCCTGAAC TCCTAGCACC TACAGGACT CCATCCCTTG TGCCCCACAT ACCTCACACG

TAGACATTCC TAATGAAGAT TTGATTGAAT TATTGTAAAC TCAGTGCCTC CCACTCTTCT

AGTTGCCTCT CTGCCTGCCT TTGTACATTT ATTTATTTAT TTATTTATTT ATTTATTTAT

GAGACAGAGT CTTACTGTAT CACCCAGGCT GGAGTTTAGT GGCACCATCT CAGCTCACTG

CAACCTCTAC CTCCCAGACT CAAGCAATCC TCCCACCTCA GCCTCCCGAG GAGCTGGGAC

CATAGGCACG TGCCACTATG CCCGGTTAAT TTATTGTAAT TTTTGTAGAG ATGGGGTTTC

ATCGTGTTGC CCAGGCTAGT CTTGAACTCC TGGACTCAGG CGATTCGCCC GTCTCAGTCT

CCCAAAGTGC TGGGATTATA GGCGTGAGCC ACCATGCCCA GCCGCTAGCA CTCATCTTAA

TCGTATATTT ACTTATCTGG CTTTCCCACC AGACTGCGGG CTCTTCAAGA GTAAATGCCA

TGTTTTCACC TTTATTTCCC CAGTTTGTGG CACATTCTAG GCACTCGCCA TCATGAAATA

FIGURE 16 (20)

AACCTCTGGA GCTGTGATAT TACAAACGTG AAAAGATGAC GAGCACTCAG CAACTTTCAG

TGAGTAAACA AAGGCTTTCA TTCAGCATGT ATTTATTGAC TGCCCTGATC TGGGCTGCTT

CCTGTCTGTG GTTCAAGGAG AGCATAGTCT ACAGAACCAG AGACCTGGCT ACTCTGGAAG

TTAGACTTAA GCCCACCCCG GTCCTTGAAT GGGGAAATAT TTCCCTTCAT TCCTGTGTTT

TAGGGACAGA AAGATGAGTA ATGCAGTGAT ACATGCTGGA AATGTTTATT CCACTACCCG

AAGCTGCCTC TCAACTTAAC AATCCATGAA AGAAACAAGA TGGTATATAA CTTTTTCTAA

TTTGTGATGC CTTTGTTTAT TTGTTTCCGG TTAAAAGAGG AGGTGGCATT GAATTGTTTG

TTTGGTTTGG TTTCTTCTTC AATAAGAAGC ATCTTAATAT AACTAGACTG GACATCTGTC

CCATTTTCAA AAATTACAAG TTTCGATCAT TGCTAAATTG TACAGATCCC AATCTGTCTG

CTCTGCATAC ATTTGCATTT ATAAAAGCAG AAGCAGACTA GCAGTCTTTC TAATGCAATC

CCCCAAATGC ATGAAGTATT AGATTGCTTC TCCCTATTGG TTCATGCATT GCTAAAGGCT

FIGURE 16 (21)

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TAAAAGGATC ATTGATTTTA ATTATTTAAT GTGTACAGCA GGCTGAGCTT CCTTTCTTTT
TTAAGGGAAG AACCTTCAGG GGCATTGCTT TAGTTTTTTA ATGTTAAATC TCATTTTTCT
TTGAAAATAA GAAGTTAAAG CTGTATTCAC ACAAGCTCTC AAAGTGCCAG ATTTTCATTG
TGTTTTTAAA CCATCTAGGA AATGTTTGAT TCTAATGAAA CATTACTGCT GAAAATTGGG
CTGAAATTGC TGGGCTGAAA ATATTGTTAT AACTTCACAT GATTCCAGTG TTGTATTATT
ATTTTTTCTT TTCCTTTTTT TGACCCGATA TAGATGAAGC GAAGAGACAA GGGAGCAATC
CCATGTGTAA TAAAAAAAGG CAGCCTGAAT TGTTGTTGCT GTTTTTGAAA TTTAAGCTGG
TTTTCAATTA AATTCAGTAA ATGGTCCAGG ACTATAAATG TTGAACATTT TTTACCGTGT
GATTTAAAAT TTAGTTTTAA TGTTTTTTTT TTGGGTTTTT TTTTTTTTGA TGGTTTACAT
TTTCCCCATG GAAAGCAGCT ATGTCATGTC GGCATGATTC ATCATGGTAA CATCTCGGGT
TATTTTGGTT TGTGTTATGT TCAGAAAGCG GAATGCCAAA AATAAAGAGT GGTTTGTGAT
```

FIGURE 16 (22)

GTCTAGTGTG TCTTCCTTTA ACAAATCAAA GGCTTTTATT TAATCCACTT AATGGGACAC

TGCAGAAATT TAAAAAATGG AAGTCCCATC CACAGAAGGC AGGTACTATG ATGTAAAAAG

TTTAGGTGGG GGATTAATAG AGTGATCATA TAATTTATGA GCTAAACCGG AGGCACTTTT

TTTTTTGAGA TCGAGTCTCA CTGTTGCCTA GGCTGGAGTG CAGTGACGTG ATCACAGCTC

ACTGCAACCT CCGCCTCCCG GGTTCAAGCG ATTCTCATGC CTCAGCCTCC TGAGTAGCTG

GGACTATAGG CGCCCACCAC CATGCCCAGC TAATTTTTGT GTTTTTTGTA GAGATGGGGT

TTCACCATGT TGGCCAGGCT TGTCTCAAAC TCCTGACCTC AGGTGATCCG CCCACCTCGA

CCTCCTAAAC TGCTGGGATT ACAGGCGTAA GCCACCATGC CTGGCCCAGA GACACTTTTG

AGAGTGAAGA GGAAGCTGAG AATAATTCAC TGATCTACAA CTGGGACCAT CCAGGGCAAG

CCAGATGCCA TTACCACTAG CTAGAAAGCT TGCCAAGGTC TCATTTACCT TGGTATATAG

CAAATTCTTC TTTGAATTCT GGAAATTCTG GTAAGTCATT GAGGTAGCTC TGTGCCAAGG

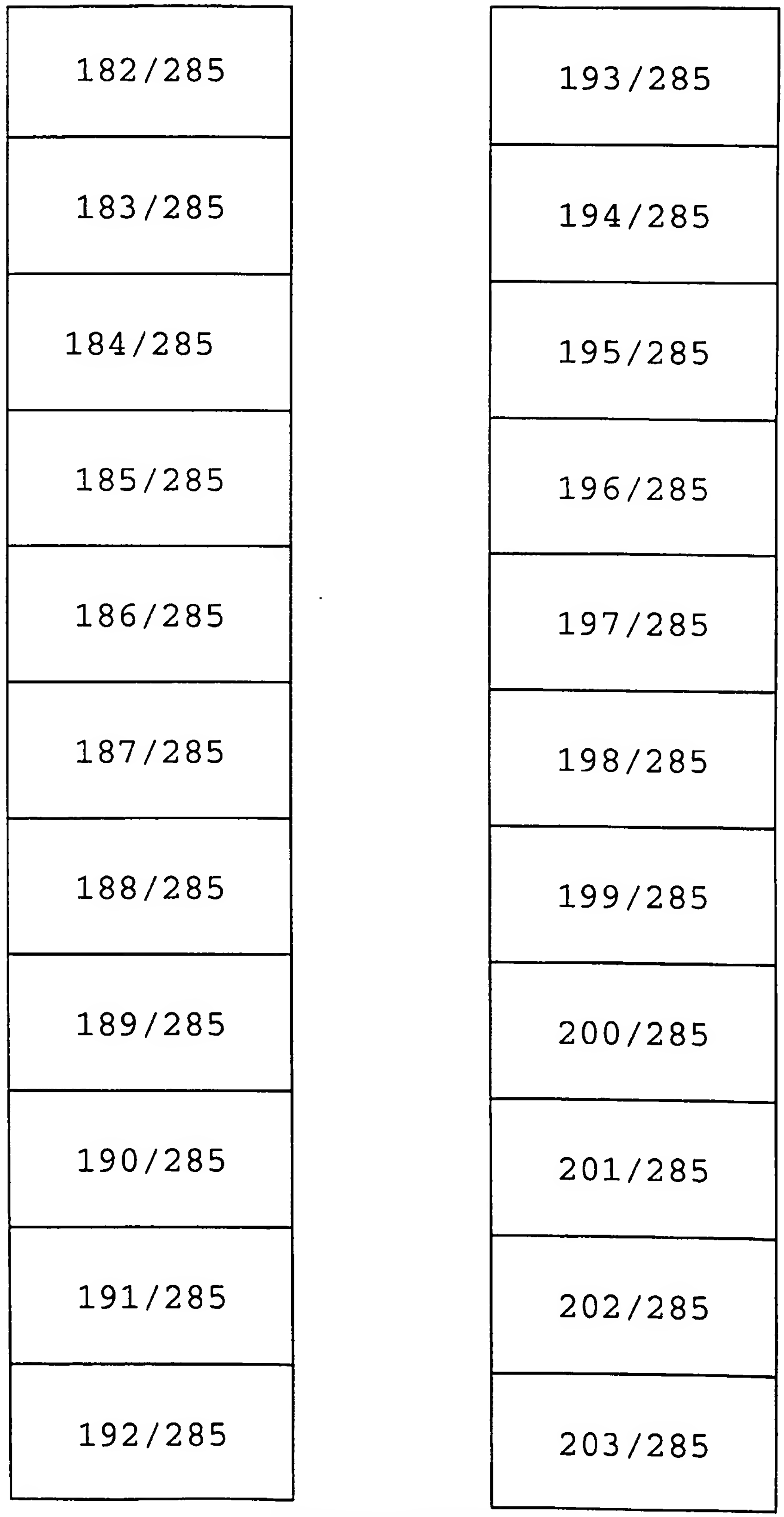
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FIGURE 16 (23)

AGCAATATGG TAGAATTCTA ATATTTCAGG CAGTACAACA CTTTCCTGCA TTTGTAGCAG

GTAAAGGGAG GTCAGGGCAG AAGACAAAAC CACTGGGACT CGACAAAGGG CATAAACGTC

TAATGCACCT GATGTAGCTG ATGGTAAATT GTTATCAGCT AAAGATCTTT CATAATAAAT

AAACTTATCA TTTGTAGGAG GGCACAGAAA TCGTGGAAAG CTGGGATTCA GGTTGCCTGT

GGCTTTAATT CTGGAATCAG AAATATTAGT CAAGGATATC AGTCTATGAA GTAAGTTTTC

AATGTTATAT GCCACAAGAT GCAGCTGTCC TATTTTCACT TCCAGTAATT CCTTCTGAAT

TAATACACCT TAAAAATAGC TGCAGCTTCT CAAATCTGTG AGAATCGTAT GTGCTGCTTG

CTACACTTTC CTTTTTCCTG AAGGCCTCTT TGAGGTCTTT CAAGAACTCA ATTCAATTCA

GCAACAATTA GGGGGTCTAA GGTATACAGA CGCTGTGCAA GATGCTCCTG AGACACAAAG

AGGAGGTCAA GCCCCTGCCT TCAGGCACCT CTCTATAATA TAGGAGGAGA AAGAGAAGAA

ACACTAATAC ACATAGGTAG GTGCCATTAA AAGGGTGCAT ACATTAAAGC CAGGTGGTAG

FIGURE 16 (24)

GTGCAAGAAG ATTTGTAACG TGAGAATTTT CTGCATGTTT GAAATATCTT ATAATTTTTA

AAAATTAAAA TGGGAGATAC ATATATATGT ATTTATGTAT GTATATATGT ATGTACATAT

ACACACATAT ATACATAAAT ATATACATAA ATATGTATAT ATGTGTATAT AGACATAAAT

ATGTATATAT GTGTATATAT ACATAAATAT GTATATATGT GTATATAGAC ATAAATATGT

ATATATGTGT ATATAGACAT AAATATGTAT ATATGTGTAT ATAGACATAA ATATGTATAT

GTGTATATAG ACATAAATAT GTATATATGT GTATATAGAC ATAAATATGT ATATATGTGT

ATATAGACAT AAATATGTAT ATATGTGTAT ATAGACATAA ATATGTATAT ATGTGTATAT

AGACATAAAT ATGTATATAT GTGTATATAG ACATAAATAT GTATATATGT GTATATAGAC

ATAAATATGT ATATATGTGT ATATAGACAT AAATATGTAT ATATGTGTAT ATAGACATAA

ATATGTATAT GTGTGTATAT AGACATAAAT ATGTATATAT GTGTGTATAT AGACATAAAT

ATGTATATAT GTGTGTATAT AATAATGTGT GTACATATAC ACACATATAT ACATACATAA

FIGURE 16 (25)

ACATTCTGCA TTATACCATT CACTTTGTAA CCCATCTTCC CTAAAAACTG TCTCATAAAG

AGTCTTCTTT TCCCTGTACC TATGCAATGG TAAGTAGCAA AACACACATT CTTTTGGGTC

CCCATAACAT TCCCTGTAGT TTGCCCTTAA CAGTCTTTGA TGTGAAATTT ACTGTTTCTG

TCTTAACCTT GCCTGTCTCG CGTACATGGA GTTTTGGCTC CTGGCTCCTA GTCTGCATCT

TCACCCCATC CCTTGCCCAA AGAATCTGGT TATGTGACCA CTGCTCATCT TTTCTGCTGT

CACAACTCCA GTCCAAGCCA CAAACCTCTC TCTCCTGGAC TCCTGCGGGG AGTTCCTTTC

TCTCCCTGCA TGAGTCTATT CTCCGCACAA CTGGCAGAGG TAAGTGAGAC TGCGGAAGAG

GCAAGTTTGC AAGTCCAGAG GAAATGAAGA CTCTGCTTGT GCACATGCTG GGTTTGACGG

GTGCTGGATA TCCGATGGAT GGCCCTTAAG GTGAGCTCAA GGCTTAAGGG AGAGATAGGG

GCTGATGATC TGAGATTCAT CAGTGTGTGG CTGATGTTTA AACCCAGGGG ACAGGATAAG

AAGGTTATTC CAGGGAGAGC GTAGATAAAG AAGCTAAATG GCTTCTGGGT CCTTAGTCAT

FIGURE 16 (26)

TCAAAATCGG ACCTCTGAGG CAGGAGGAAA GCCCAGAAAG AGTAGATTCC TGGGACTCAC

GGGATAAAGA CTTTCAAAAA GTGGGGGCTG GCCAGTGCTG CTGAAGGAAG TAGCAGGACC

GGAACAGAAG GGTAATCGTT GGACCTGGAG AACTTGAATT TGAATTTTAA GGTTGGTAAC

CTTAAAAAAG AGCAATTTTA GATACCTTTT GAAATTATTT GCAAGATTTG TTTGGTATAT

GTGTTATTCC AGGCAAAGGG ACCAGAAAAG TAAAAAATAC TTACTGAACA GTTACTGCAT

GCCTGGCACT GTAACACCCT GTTTAATTCT CACGGCAACC CTATAGAGTA GGTGTCATCA

TCCCCATCTT ACAGATGAGG ATATGAGGTG CAGCTAGATT AAGCAGTTTG CCTCAGGTTA

CACCAACTGG TTAACGTAGA GCTAGGATTT GAACCCGGAT GGGCTGATCC CAGAGCTCAT

GCTTTAAATC GCTAGACTGG TGCTCACAGA AGACTGGGAC CGAAAAAAAT TAATAAAAAA

AATAAGGAGC CCCCTGGGCT AGCAAATTAG GAGTTGTTCA GACAGATGTG AAAAGGAAAG

CAAGGCAGAG GGAAAGTCAC TGTACAGAAG AGAGAGACCC ATGACAGCAG AGACAGTGAG

FIGURE 16 (27)

CTGGTAAAGT GGCTGGCGAT CTAGCCCCTG AAAATACCTC CAGAGAGGCA GGCTCACGCC

TGTAATCCCA GCACTTTGGG AGGCCGAGGT GGGCAGATCA CCTGAGGTCA GGAGTTTGAG

ACCAGCCTGG CCAATGGCGA AATCCCGTCT CTACTAAAAA TACAAAAATT AGCCGAGCAT

GGTGACAGGC ACCTGTAATC CCAGCTGTTC AGTTGGCTGA GTCAGGAGAA TAGCCTGGAT

CCGGGAAGTG GAGGTTGTAG TAAGCCAAGA TTGCGCCACT GCATGCCAGC CTGGGCGACA

GAGCAAGACT TTTCTTAAAA CAAACAAACA AAAAAGAAAA AAGAAAAGGA AAGAAGAAAG

AGACAAAGAA AGAAAGAGAG AAGGAAAGAA AGGAAGGAAG GAAGAGAAGG AAGGAAGGAA

AGAAAGAAAA GGAAAGAAAG AAAAAGAAAG AAGAAAGAAA GGAAAGAAAA GAAAGAAAAA

GAAAGAAAGA AAATACCTCC AGAGAGCCAG GTCTCTTAGG CCTTCTGAGA AACTCACATC

CCTTTTGATG AACACAAATG CTTCACACTC TCAATGTTAT TGGTAATCCA AGTTATCAAT

ATACCTAAAT CACTTAGTAC TGAATCTGGC ATATAGTAAT CACCTAATGA AGAGATAAGA

FIGURE 16 (28)

GTCATGGAGT ATTCTGAAGC AATTAGAATC AATAGACTCA ATATACACAT GGCAACAAAG

TTGGATCTTA AAAACCGACC TGAGTGAAAA AGGAAAGGGA AAGATACATA ACACGGTACC

ATTATGTAAA TTGATAATAT ATGCTTACAC AATTTGTAAG AACACATACA AATAGATACA

TGTATATTAA ACATACTCGA ACGGTTACCC TATGGGGTGG TGGCTGGAGT GGGGGTAAGT

CCGTAAGCTG TAATGGAACC TAAACAAATA CATGAAACGA GTAGGAATCA GAAGGAGTAA

CAATAAAAAT GTGCCATGAA CTGAGGAGTG TAAATTAATC AACTCACTGC ATCTGAGGTT

AAAAATAGAA AGATGATAAT TGTTATTCTT ATTACTCCTA GGTCTTCCAC TTGCACTCAG

CTTTACAATG TTGGACTATC CTTCAGATGG CACCCTCCTT GCACTTGCTC AGGCAGGAGA

GCTTTTTCCT CCAGCTTTCT AGGTGATTTA ATATATCAGG GAATAAGTAT AAAAAAAGGC

ACGGTGCTCC CTGGGTAGCC TTTCTGGACT TCAGAGCTAA ATTGCAAAGT CAGTTTTACA

CATGTGATTT CATCTATGAA ATTAGGGCAA GGTATAAAAC TGGCACAGAA AAAATGTGAT

FIGURE 16 (29)

TTATTATGGT GTTACTATCC CTTACAAGCG GAGTGTCAGC TGCCTCTTTT TGTCCACTGA

TTTAAGGCAA GATGAACTGA AAGTGGCTAT GATCACGTCT TCAAAAGCAC ACTCTGGCCC

CTCGGCTGCA GGCGCCCTGC ACATTCCCCA GCTGCGTGTC CGGTGGTGAC ACAGTGCATA

ATTGTGGCGC CTTCCTGGTG CAAACTGTCT CACTTAGCTC CGTCTTGCTG GCACAGCAGA

AAGGAAGAAA TCGAAAATGT TTGGATTTCA AAGGTAACAA GAAGCTGGAA AACAACTACT

GGCCGAGTCT GAGAGTTTCA GCGGAGACTG GTGCAGCCTT GTGTTTTTCC ACTGACAGCT

GAAAATGAGC CCAGCTTCAG TGAAGCTTGT TTCCTTCCCT CCTCAAGGTT ACCCACAATT

CTCAGTTCTC TCAGGAAAGC CAAAAAATGA ATTTGAGGGT TTAGGATTGT GGTTCTTTTA

TCTATTACAG GATTGATAAT ATGTTCCTCC ACCAGATGTT CTGCTTGTAA CAATACTCAC

TTCCTGACAC TACTGCATAT GCAGGAGTGT CACTACCAAG GTAAACACAG AATTGGCTGC

CCAATTCCAA ATCCCTGAAC TGAGTGAGAG AAATCAGAAT TATAATAGGG GATTCAACAG

FIGURE 16 (30)

AGCTGGCTAC GGATGTGCCA GTGGTCAGAT ACTTTGCTCA TCATACGCAG GTGCTGCTGC

TCTAGCAACT GCTCACTGCT TCATTTCCTG CCTTGGTCTT TAAATACTGC TTTTCTCAGC

TCAATTGGCT TTCTTCCCTC TGGCAGTCAC GTTTCTTTGG GTCAAACAGC AAATGATTCT

TTAGAATCAC CTGGTACTCA AAGGAGCTAC AAGACATTGG GCATCCACTT CCACTCTCTT

GGAAAAACAA TTTTATGGAA GCCAAGGTTG CCATAGTGCC TCTTGAGGTT GTTTGCTCAG

CCAAGGCCCA AGCTTTGTGC TTCAAACATG AAATTAGAGA GCTTCAGAAC AAGATCCACA

TTTTCAATGG CCTCACCCAA CTGGATAAAA GAACAATTGC CATATCTCAA TGACCACCTT

TTCTCAGGTG GGATGGTAGA TGCTGGAATG GGTCACAGCA TTGCCCAACC AAACTTTGCA

AAAAAGGCTG GAAGCTCTGA CTGGGGACCC TAAATATGCA AAAGTTAATA GGCTCTTCAT

GCAGAATATG AACCCCGTGT ATGGATATAG CTAAAGGGTT GGCCTTTATG TTTCTATTCC

TTCACAAACC TGGTAGAATA GATATGCTTG TTTCCCTTTA AAAAATGTCA ACAATTGCAT

FIGURE 16 (31)

TTATGATGCT GTGTATAGTA ACTCACAGAT CATGCTCCAT GAAAATGCTT CAGAACCCAA

TATAAGGAGA TTTTTTAGCC ATGTGTGACA AAAGAGAGGC CATTTCAGTG TTGAAATTGT

TCAGAGAAGT ATTTGATTAT GTTTTCTCAG ATCTTTTTAT TTTTATTTTT TTTGAAACAG

AGTCTCACTT TGTCACCCAG GCTGGAGTAC AGTGGCTGTG GTCTCGGCTC ACTGCAACCT

CTGCCTCCCA GGTTCAAGCG ATTCTCCTGT CAGCTTCCCG AATAGCTGGG ATTACAGGCG

CATGCACCAC CATGCCTAAT TTTTGTATTT TTAGTAGAGA CAGAGTTTCG CCATGTTGAC

CAGGCTTGCC TTGAACTCCT GACTTCAGGT GATCCACCCA CCTCAGCCTC CCAAAGCACT

GGGATTACAG GCATGAGCCA CCGTGCCCAG CCTGTTTTCT CAGATCCTGT ATTTTGTTTC

TGAAGCCTTC ATTTCTATCT TCTTATTCAT TTTGGAAGTA GTACACCTAA GTAAGGTTTT

TAACAATCAA ATATCTTTGG AAAATTCCCT GGTTCCTTTC TTATTCCTAC AAAAATATGT

TCAGTATAGC TGATGTTATG TTTCTTTCAA ATTATTCATT TCTCTATCTC AGAATTTATC

FIGURE 16 (32)

TCATGCCTAA TTGTTATTGA ATAGTCTTCA CTTCTTGTCA TCCAGTTTCT GGTCTCTTAT

TTCACTCTAA GTCTAATTGG CTATTAGAAT AAAGAGCTTG TAACAGATTC TTTCTCCAAT

ATGTCTTATC TTTTGACTGC ATGCCAGTGA CAAACTGTTA ACTGTTTTGA TTCTTCATAA

CATTCCACAG AACATGCTGA CTCCTCTCTT CCTGAAAGCA ATGCCCAAGC ACAGCATTGT

TAGATAGTAT GTACGCAACA GGGACATGGG TGCATAGCAA AAACTAGAAG GAAGGAGGAC

CTTCCTTAGC AATGGGTGAT ATGGTCCCTG GACTTAGACT CCAAAGGGTC GTGAGGTGAA

ACACACATCG TCCATACCCA GGAAGCACAC AGGTGGGATG GAAGAGCTGT GCCTAATGAA

ACTTCATCCA CGTGGAGGTG GAGGAGGCTG CAGCTGCAAG AACTCAGAGC TGCCTTACCC

AGACCAGGGA CCAGGGAGGG CTTTCTGGAG GAAACAGCCT CTGAACTGCC AGCTGATAGA

GGAGCTCTAC CTCAACTCTT CTGGTTCCCC AGGGCTGCTT TTCCACGTCC ATTTATTGGC

ACTGAAGTTT GAATACCTTC AGGGGCCCGA AAGCCTGCCA GGTCCTCTTC TCTGCAGAGC

FIGURE 16 (33)

AATCACACCA ACCTGCAAAG GGCTAGGAAA GGGCTGTCAT CATCTCCTAC TCAGAAACTG

GTTCACTGGA AGGACTCAGG GGCCACTGAA TACATCCTGG CAGCTTTCAC AAGAAGGGCT

TCTGACTCAA GGATGTTTCC ATCTTTGCCA GGTCGCCTTT TCTCCTTCTC TTAGAGTTTG

GAGGACGCAA ATGTGCTGAG AAGTCAACCT TTCCTGCAAG GTGAGACACA AGGGCCTTTC

CCAGCAGAAA GAAGAGAGCA AATGGAAGGT CCTTCTTCCT CCAGTAGAGG ATGGACTCTG

TCTGGCAGCC ACCCAACAGG AAAAGCACAA TGCATGCCTG CCTGCTTCCC TCCCTCCCTC

CGTTTCTCCC TCCCTCCCTC CTTCCTCCCT TCCATTCTCT TCCCTTCCCC TCCCTTCCCT

TCCCCTCCCT TCCCTTCCCC TCCCCTCCCC TTCCCTTCTC CCTCTCCTTC CCTTCCTCTT

CCCTTCCTTC CTCTTCCCTT CCTTTCCCCT CCCCTTCCTT TCCCTTCCTC CCTCCCTTCC

TCCCTTCTTT CCTTCCCTTC TTTCCTTCCT CATTTCCTCC CTTCCTTCCT TCCTTCCTTC

CTTTCTTCCT ACTTTCCTAC CTTTAGGGCT CTGTGTCTTT GGAGTCCATT CTGATTATGC

FIGURE 16 (34)

TGTAATGTCT GCCCCTTCCT CTTCTCTGTC AAAAAATGAA AGACATGGAA GCCACTTGCC

TTTTACTGAA TTAAAAATTA GTAAAAGAGC TAAAAATTAA TGGTTAAAAA TGTACGCATA

AATTATGCAG TATACTAACC AATGAAAAGA TACACTTCTC TTAATTAAAA GCTGACAGGG

AGGGAAACAA GAAAAGAGAA ACACAAAACA ATAATCTAAA TGACCTATTA GTTGGAAGAA

CAACATCAGA GAAAATAGAT ACTGTGTATA GTCATGTGTA TGTCTATGGA ATAACATTTG

TAGAGAAATC TGGACTGATC CTTTCTGAGT AAAGAGAGCT GTGGGTACAA TTAAGGGGAG

ATTGAAAGGA ATCCAAAAGC ATAGCAGATG CTGTGCCTCA CTGGAATGGT TGCCGATCTC

CTCCAAACTA TGAAGTGTTT GAGGCTCAAC TTTAATATAA TTAAGATACA AAGACAGAAT

GAGAGAAAGA GAGAAGGGAG CTCACTGGAA GAACACTCAA GATTCCTTAC TACTCATTCT

CTAAAATTAC AATTGTTCTA GATGGAAAAG AAAAAAAGCT TCTCTGTTAA AAAAGGAGCT

TGTGCTATAG GAGGTTTAAA ATATACTTCT GACCCATCTC CAACATTCTA AATCCTTCCC

FIGURE 16 (35)

AGAAAAGTAT GCCAATCCCA AGAAATATTC AATCAAATTG CTGGAAAGAA AAATACAAAA

TATTAAAATG TATTAGGAAG CGACAGTAAT TAAATCAGAA CTGGAGCAGG AATAGACCAG

CAGATCAATG AGACAGACAT CAAGTCCCGG AATGTGGACT TGCAAATGCA TTAAGTAATA

TGATATGCAA TAAAGGTGGC ACAGTGAACC AATGGGAAAA AAATTAATCT TATAATAATT

GATATTGCAA TAATTGTCTA GTAATTGGGG GAAGAAATAA GCTTATTCCT TATCTCATTT

CTTTTTTTCT TTTTGAGACA GAGTCTCACT CTGGTAGCCC AGGCTGGAGT GCAGCGATGC

GATCTCTGCC CACTGCAACC TTGCTCTCCC GGGCTCAGGC GATTCTCCCA CCTCAGCCTC

CCGAGCAGCT GAACTACAGG CGTGTGCCAC CACTCCCGGC AATTTTTTTT TCCATTTTTA

GTAGAAATGG GGTTTCACCA TGTTGCCTGG GCTGGTCTTG AACTCCTGGG CTCAGGCAAT

CCACCCGCCT TGGCCTCCCA AAGTGCTAGC ATTACAGGCA TGAGCCACCG CGCCTGGCAG

CTCATTTTTT AGACTAAATA AATTGGAGAT GGCTAAAAGA TTTTTATGTA GGCCAACTAT

FIGURE 16 (36)

GTTTTTAAAA AGTTTTTTTT TTTAAGGATA TCTGCTGGAA CCAATCATGC CACCAACCAA

AGATGCAAGA CTATAAAACA TACCCAGTTT TTCAAAGCAT TTAAAAATTA TTCTAAAAAT

ATTTTTTCTC CAGAAATTTT GCATTGATTC CCTGAAGAAG CATTAATATG GGACCTGACT

TATAAAATGA TGAACTCAAT CTCCCCACTC AAGGTAGGAG TCTCTCAGAT TTAAAAAATA

AGCATCCTAG TCCTCTTGTC CCTGTAAAAG TTAACCCTTA CACCTGAAAC ACCAGGAGAC

TGGCGGTTGT TTGCATAGGG GTTACAATTA AAGTTGAGCT ACCTCTGACA TCTATTAACA

CCAAAATTAG TAAACTATGC ATGTATGGAG ACTTTTATGA TTGAACTTGT TTATTGAGTC

AAGAGATATA GTTTACAATG AAAATTTGGG GCATATCAAA ATGACCTTGG CTTAGCTTAG

CATTTGCTGA TGTTAACTAT TTTCTTCATT GGGCTGATTT TAGTTGCTTA GGAAAAATAC

AAACACACAC ACTTTAAAAT TATATTAAAA TCCCGTCCTA AACCTCAGAG TCCAGAACCG

CATCCTAACA CTGGTCATGC ATAATATGTT TAAATTTTTG TGCTTTAAAA ACTACAAATA

FIGURE 16 (37)

AGGAATGTAT TAATAGTTCC ACAATCAATG GTCAGTTAGC CGAGGGAAGA TTAGCATAGT

TAAAGACTTA AAATGGCTTA ACAACATATA TCAAAAGGAC AAAATAAGGG GAACAGAGTC

TAGAAATGAG GAAACTGGGA CACAGGCAAA AAAAAAAAAT GAGAACTGGG ACATGAATAA

CGCAAGGGAT AAGACTAATA CACAAAACAC CCCAAATAAA TAGCCAGCAT TTGCTGAGCT

CTTACTGTGA GCCTGTTCTA AGCACTTTAC ATATATTAAC TCATTTCATC CTCAAGGAAC

CATCTGAGGC AGGCACTGTT ATCATCTCCA TTTTACAGAT AAGGAATAGA CCCAGAGAGG

CTGAGCAACT GGGCCTATTC CACAGCTACT ATGGTGGAGA TGAGATTTAA ATCTAATCAT

TGGCTCCAGA GCCCATGCAC CCAATGGCTG CACTAAGTGA ATGCATGCGC TATCAACGTT

GCCAAAAGTG GGCCACAGCT CGGATCTGCG TTTTCCAGTA GCCAAAGCAG AGAGTGTGAT

CAGACCTCAC TTTAATAAGC AAGTCTCAAG CCAGAGAGAG GTGGTATCAG GCAGCAAACA

GGCTGCTAGT CGAAATCCCA CTTCTTCTCT GAGTGGTCCA TACAGTTTTA CTCTACTTGC

FIGURE 16 (38)

TTACAGAATG AAAATAGCTG GAGTTCAGGT GCGCTTTCAA TGCCCTGTTG TCAGGATTGG

GCTTTTCAAG TTTATTTTTT GTTGTTGTTT TTAATAGACT GTACTTTTTA GAAAATTTTT

AGATTTACAG AAAGATTGAG AGGATAGTAC AGAGAGTTCC CGTATACCTC ACACCCAGTT

TCTGCAATTA TTAACCTCTT ACATTCATGC GGTACATTTG TTACAATTAA TGAGCCAGGG

CCGGCCGGGC ACAGTGGTTC AGGCCCCTAA TCCCAGCACT TTGGGAGGCA GAGGCAAGCG

AATCACTTGA GGTCAGGAGT TCGAGACTAG CCTGACCAAC ATGGTAAACC CTTTCTGTAC

TAAAAATACA AAAAATTAGC CAGGCATGGT GCTGGTTGCC TGTATTCCCA GATACTCAGG

AGGCTGAGGC ACAAGAATTG CTTGAACCAG GGAGGCGGAG GTTGCAGTAA GCCGAGATCG

TGCCACTGCA CTCCAGCCTG GGCAACAGAG CGAGACTCCA TCTCAAAAAA AAAAAAAAAA

AAAAGAAGGA AGGAAGGAAG GAAAATTAAT GAGCCAATAT TGAGACATTA TTATTACTAA

AGTCCATGCT TTATGCAGAT TTTCTTAGTT TTTACCTGCT GTCATTTTTC AGTTCCAGGA

FIGURE 16 (39)

ATGCATTCAG GATGCCATAC CACATTTAGT TCTCATATCT GCTTAGGCTC CTCTTGGCTA

GACTGAGTTT TAATCTACTT TCTGCAGAGC CTGAGAACTT TAGCATAATT TCCTTGAAAT

TACAGCTCAA TATTTTCAAG CACTTATACA AACAGCCTAA TGTTACGTTG GCCCATAACA

GTGTTTCAAG GTAATAAACT TCTTTGTTTT CTGTGCCGAT TGAAAGAACT GCTGCTTAGC

CTCCTGCCAG ATGATGAACT GGGTACACAC GAGCATTTTT CCAGGTAAAG CATATTTCGT

GCGACTTCTT AAGCTGCAGC CTTATATGCA ATAATTGTCC ATTTACAAGA CTTATGTTCG

AATTTCAGGC ACTCTGTTTT CACTAACCAT ATCTTCAACT TTGATAAGTA CTGCTTTAAT

CACTCAGAAA ATTTAACTTG ACTAATTTTT TTTCACCATC AGTTTTTTTT CTGTTGACTC

TTTCTCCTTT TTCTGTTTGC CCAGAAACAT GCTCAGGATT CTCTCAGGCT TTAAAAAATG

AAAAAATGTT TCCTGCAATC TAGTTACTCC TTGATTCTCT TGTTCTGTTT ATCGCTGGAA

TTCTTGAAAG CTTGGTGTAT TAGTCTTTTT TCATGCTGCT GATAAAGATA TACCTGAGAC

FIGURE 16 (40)

TGGATAATTT ATAAAGAAAA AGAGGTTTAA TGGACTCACA GTTCCACGTG GCTGAGGAAG

CCTCACAATC ATGGTGGAAG GCAAAAGGCA TGTCTTACAT GGCAGCAGAC AAGAGAGAAT

GAGAACCAAG GGATTTCCCC TTATAAAACC ATCAGATCTT GTGAGACTTA TTCACTACCA

CAAGAACAAT ATGGGGTAAA CCGCCCCCAT GATTCAATTA TCTCCCACCG GGGCCCTCCC

ACAACACGTG GGAATTATGG GAGCTACAAT TCAAGATGAC ATTTGGGTGG GGACATGGCC

AAACCATATC ACCTGGCCTA TAGCATTATT TCCATTTCTT CCCCATCCTT TTATTCCTCA

AACCGGTACA ACCAGACCTC TTTTTTTTTT TTTCTACCTG AAACTGCTCT TTTGAGGGTA

GCTGATAAGT CCAAAATACT GTCACCTTTT CTCAATTCCG TTCCTTCTTA TGCCTTTGGA

GCAATTGACT GTGTTGGTTG CCCCCTCCTT TAAAGTGTCT CTCACTTGGT TTTTATGACT

AATGATCATG ATTTTCTTTT TCCTCTCTAA ACATTCCGCT ATCTTTTTAG CTTCCCTTCC

CCCTCCCATC CCCTAAATGT CCTTGTTTCC CAGAATCTGC CTCACCTCTT TGACTTCTCT

FIGURE 16 (41)

ATGCCCTGTC ATTCACTCAT GGGTCTTTAT TACATTATTG CATCTGTGTC AATAACTCTG

GTCTTTCTCT TAAGTTCCAG TCTCCCATTT TCAAATGTCC CCAGACATTT CCAATTGAGT

ATCTCTCCAA TGTATTTAAC CTGCTAAATA TCTAACACAT AATCTTTCCC ATCAAATCGT

TTCCTCTTAA GCTTTTCTTA TTTCCTATTA GTACTCCTGC ACTTCTCCCA GGAGCCCAGA

CTTAAAACCT TGAATTTCTC ACCATAACCT CTCTTTTGTC TCCCATAATC AATTAGTAGC

AAGTGTTATC AATGATTACT TGACAATATC TTTTTCTATT TCCCTCCCTG CTATGATCAT

TCATCTAGCA AGAAGAGTTG GCCCTTTGTA TCTGTGGTTT CTGCATCCCT GGATTCAACC

AACTGTAGAT GGAAAATATT TGAAGAAAAA AGCGTCTATA CTGAGTATGA AAAAATTTTA

TTTCTTGTCA TTATTCCCTA AACAATACAG TATAACAACT ACAGCATTTA CACTGTAGCG

TATAGATCTT ATAATCTAGA AATGATTTCA AGTACACCAT TATATATAAG GGACTTGAGC

ATCTGTGAAG TTTGGTATTT GTGGGGCATA CTGGGACCAA TTCCCCCATG GATACAGAGG

FIGURE 16 (42)

GACAACTATA TTTACTCAGT GCTTACTAAA TACCAGTTGG CCAATGTGTT TTTCTTTTTC

TGTTTTCCTG TCTTTAGTTT GCCCCTTGCC AATTAATTCA ATAGTGCTGC CAATGCCAGG

TGTACCTTCA GAATATTCTA TTCTAATTTT GTCATCTCCA AGCTTAAAAA TATTTAATGG

GCCAGGCGCA GTGGCTCACA CTTGTAATCC CAGCATTTTG GGAGGCCAAG GGGGGGTGTA

TCACTTGAGG TCAGGAGTTC CAGACCAGCC TGGCCAACAT GGCGAAACCC TGTCTCTACA

AAAAAGTATA AAAGTTAACC AGGTGCTGGA GCATTTGCCT GTGGTCCCAG CTACTCACGA

GGCTGAGGCA AGAGAATCGC TTTAATCTGG GAGGTGGAGT TTGCAGTGAG CCAAGATCTC

TCCACTGCAC TCCAGCCTGG GTGACACAGC AAGACTCTAT CTCAAAACAA CAATAACAAC

AACAACGAAA AACATTTAAT GGCTGCACCT TGCCTGTGAA AAATGCATTT CTTGGCCAGA

TGTGGTGGCT CAAACCTGTA ATCCCAACAC TTTGGGAAGC TAAGGCCAGG AGTTCGAGAC

GAGCTGGGAT ATATAGGAAG ACACAATCTC TACAAAAAAA AATCCACAAA ATTAGTCAGG

FIGURE 16 (43)

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CTTAGTGTTC ATGCCTGTAG TCCCAGGTAC TCAGGAGGCT GAGGCAGGAT TCCTCAAGCC
CAGGAGTTCA AGGCTTCCGT GAGCTATGAT GGCACAACTG CACTCCATCT TGGGTGACAG
AGCAAGGTCC TATCTCTGGA GAAAAAAAAA AAAGAAGGCA TTTCTTAGGA GAGTTCTTCT
CTGTAGAGTC CTAAGGGTTC CATGGAACTC CTTAAAAGCA TCAGAGTATG TGAGTGCAAT
GGGAGGAAGC ATTTAGCCAG AGCAGTTGTG CTCCCATTGC ATATTAATTT TTAAAAAACA
AAGCTATAAA AAAAAGTTGA AAACTACTAC GTTAGCATCA GCCTGACATT TAATGGCCTC
GTAAATCAAA CCTTAATTGA CTTTTTAGCC AGTTATGCTA CTAGCCAACT ACAGACAACA
CACTTTTTAA CCAAATTAGA CTAATAGTTG TCATCAGTGG AAATCAAGTT TGCCATTCTT
CCATGCCTTT GCTCACACCA TTACCTTTTC TGGAATGTCC TGTACTCATC TTCCTGTGTT
GAACTCTATA CCCAACTTTA AAAACCTAGC TCAAAGTTCA ACACTTCCAT TCCATTTCAA
AAAGAGCTTT CCTCTTCCTT AAAGTTTAAG AACTCATTTT CATGAATCTT TTTGGCATTT
```

FIGURE 16 (44)

ATTGCACACA TGCTTGCTTT GTGTTATTTG TGTTCATGCC TCATATGCCC CCAAGGTGTT

TTAGACTCCT TAACGGCAAA AATGATGCTC TAAACACCTT TCTATCTTTC ATAGTGTCTT

AGTCTGTTTG TGTTGCTATA AAGGAATACC TGAGGCTGGG GAATTTATTT AAAAAAGAGG

TTTATTTGGC TCACAGTTCT GCAGCTATAT AAGAAGCATA GTGTCAGCAT CTGCTTCAGG

TGAGGGCTTC AGGAAGTTTC CACCCATGGT AGAAGGCAAA GGGGAGCAGG CATCACATAT

CAAGAGAGGA GGAAAAAAAG GAAGGAAGAA AGGAGGGTGC CATTCTCTTT CAACAATCAG

TTCTTGTGGG AACTAATGGG ACAAGAGGCT GGGCACGGTG GCTCATGCCT GTAATCCCAG

CCCTTTGGGA GACCAAGGTG GGTGGATCAC CAGAAGTCAG AAGCCTGAGA CCAGCCTGGC

CAATGTGGTG AAACTCCGTC TCTACTAAAG ATACATAAAT TAGATCTAGC TGGGCCTGGT

GGCGTGTACC TGTAGTCCCA GATACTCAGG AGGCTGAGGT AGGATAATCA CTTGAACCCG

GAAGACAGAG GTTGCAGTGA GCTTGTGCCA CTGCACTCCA GCCGGGGCAA CAGAGTGAGA

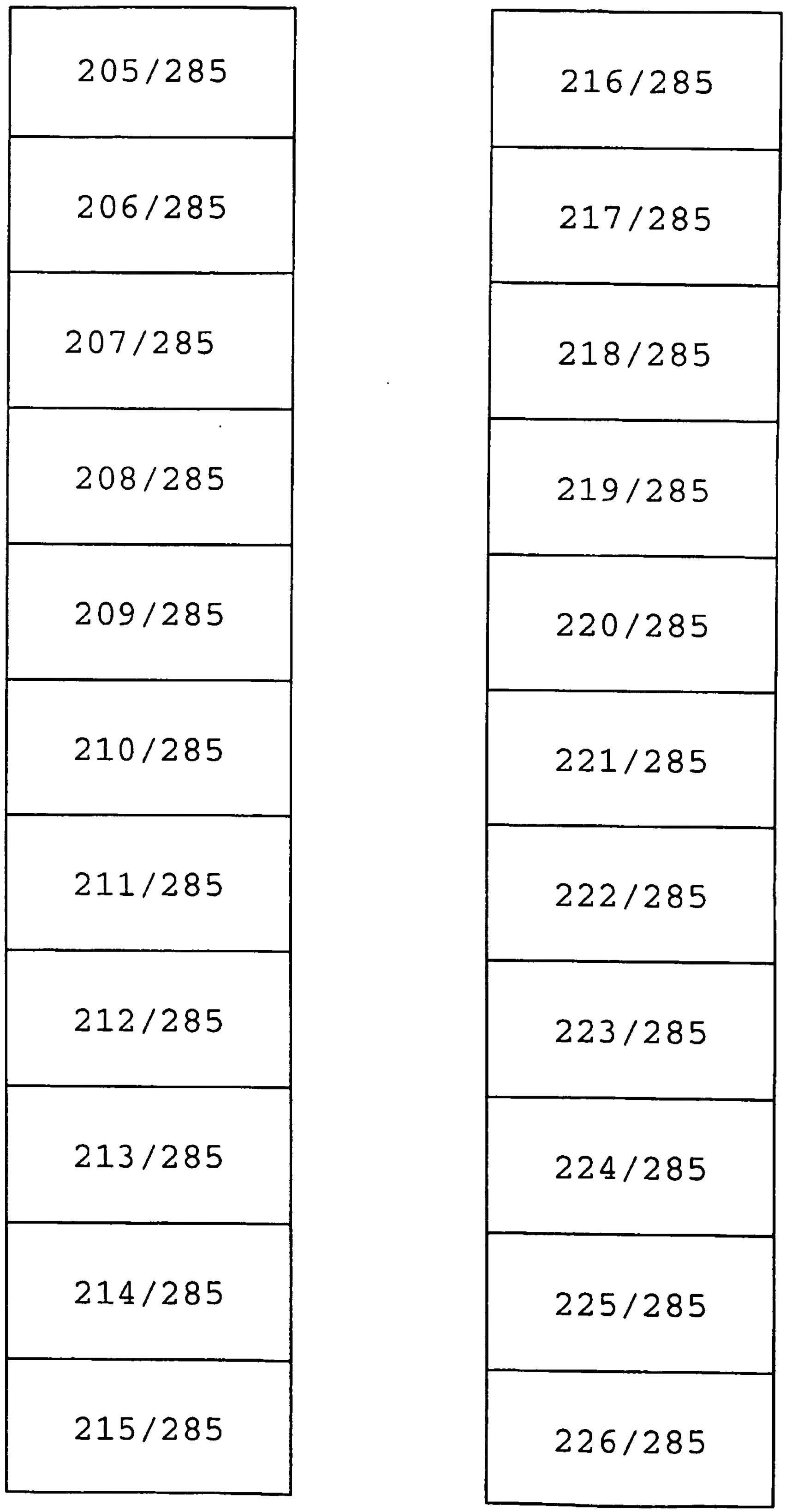
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FIGURE 16 (45)

CGGTCTCAAA AAATTTTAAA AACTTTAAAA ATAATAGAGC AAGAAAGCAC CAAGTTATTC

AGGAGGGATC CACCCCCAAT GACTCAAATA CCTCCCACCA GGCCTCACTT CCAACACTGG

GGATCAATTT CCGTATGAGA TTTGGAGGAG ACAAATATCC AAACTATATC ACATAGTAAT

GAACATAGTA CCTTATCTAT AGAAAGCAAT GGCTAGACAA CTGTTGAATG GCTAACCAAA

TCTGCTTTCC TATGGTCTCG CTCTAGAGGG GGTCAGTATG AGTTTCTGTC AAAAGGAGAA

AAAAAAATGT ATAGTCAGTT TTGTGTGTGT GTGTGTTCAT GTAAAAGAGA TCAAGAGAAA

AGAACAAGAG AAATCATGAA AAGGAGGGGG AATATAAGAA TAATACATAG AAAAAAGCAA

ATTATCTTGT TTATCAGTAA TACCCAAGGG GGTAGAAATG GTAAGTAATA ATCCTTCTTC

ACTTTGTCTG TAGTTCACTT TTTTGCACCT TTATTTTGAT GAATTCACAT CGAAGACATT

AACTCATTAA GGCTTCCAAT ATTTTTGGAG ATAAGAAGGG CTGCTATGCT CTTTATAGAT

GGAAAACTTG GGTCATTAAT AACTCAAACA AGGACATAAC AAAGAAATGG AGCATAAACT

FIGURE 16 (46)

GCCAGGTCCT GACTGTAGAT TTGGATTCCC AGTTGGTGTC TTGTCACCCT TTGTTACTCT

TCCTAAAGTT ATGATCTTTT CTTGTGCATA GGAAATTCAT AGTGATTTCC CATCACCCTT

GGGATTATCA TAGCTCCTTT AAGGTCCCCT CTATGCACTC AATAACATCA ACAGTAAGTG

TTCTTCGAGC ACTTACTGAG TGTATATCAT TGTGTTCTCA CGCAGCACCC ACAGATCTCA

CCAAGAACCT AGCTGAAGCC TGTAGAATGA ATAGGTAAGT ACTGCCATGC CAATCTGGAG

TACTCAAGCG ATGCAAATGA TTCCTTTAAT TGTACTTTTG CAGGCTTGTC AGTTTTGCTC

ATGGAGAAGT GGCTACTGCA TCCATGTTAT ATCTATGTAA TGTTGGACTG CGAAGCATCA

CTTGACTTTT TCCAAGCAGA AATTACAGCT GATGACAAGC TGCTGCTGAG AAAATGGATA

TTTTTCTGAA TTCAGTTCTA CGTGGAAACA GCTGACTAGT TTCCATTGCT GTAAGATGGC

TCTTTTGCTC TTGGTTGATT TTGAGTAATG GCTTTACTTC TGTAGAAAGG AGATTTCATT

TGAAGTCCAC TCAGGGATTT GGTTCAACAA ACTGGAGTAC AGGTTTCAGA AAATATCTCT

FIGURE 16 (47)

TTAATCCTCC AATAATAAAT TTTCTCATCT ATAATTCCTG GAACACTTCA TCCTTTGCAG

CCGAGCATAT AGATAGATTT GTTGCTCACT GTGTTCTGAT TGCCACTTTG ACCTGCTTTT

TCAACTTAGG TTACAAATAG AACAGAATCT CTCTGATTTT TCTCATTAAT TGTTTGAATT

CCCACTTTTC CTCATTAGCA AGAAGTCCAG TATCTTCCTG AGAACTTCCT TTTCTCAATC

TAGGAACTTA CTTGGTCCAT AAGGTAACAG TCTTATTTCT GACTATCAAG GAGAGAAATA

ACAGGAGCCA TTATCATCTT CATGGTGTCA CTTTTGAAAA CTGGTCCTCT GTAGATCTTC

AGATTCTTGC GTTAGTCCAT TCAGCTGCTA TAACAAAATT GCATAGACAG CATGGCTTAT

AAATAACAGA AATGTATTTC TGACAGTTCT GAAGGCTAGA AAGTCAAAGA TTAAGACACT

GGCTGATTTG GTGTCTGGCG AAGGCCCATT TGCTCATAGA TGGACGATGA CCTTTCACTC

TGTCTGCACA TGGCAGAAGG GCAAGAGAGC TCTCTGGGTC TTTTTTATAA GGGCACTAAT

CTCATTTTTG AGGACCCTGC CCCCATGACT TAATCACCTC CCAAAGGCAC TGTCTCCCAA

FIGURE 16 (48)

TACCATCACC TTGAGGGTTA GGATTTCAAC ATATGATTTT GGGGGGACAG AAACACGCAG

TCCATCTCGC TTGTCCACTC CATGGTGGTA TTCTTGCTGG ATCAGTTTCC TCCTTGGGGT

GCATTTGTGT TCCATGTCTA ACTTGCAAGT TATAGCAGGC CCGATAGCAA AGTATTCCAA

TGTTGGTATG CAGAGGCATT GAATAATCAG AATGAACCCA CGCCATAAAC AACTGGTAGA

GCTGCAGAGA GTACCAGCTG ATTATGAGCC CTGGGTAACA GTGGTTTTTA GTTCCTATGT

CCGTCAGCCC TTTTCTCCCA TAGTAGCCCC ACTGTGTTGA AGTGGCTGAA TCGACAGAAG

CTTCCAGCTT GGGCCACATG CTCATGGAAC CAATTCTCCT TATGAGCCGT ACAAGAGCTG

GGTTGCCATT CTGGATACCC TCTTTCTTCA AGAGATTTTA TTTCAAGGAT ATTTTTTCTT

TTATCAACTA CAGGGATTAT TTAGAATCTT AGGGCAGTGG TGCCCAACCT TTTTGGCCCC

AGGGACAGGT TTTGTGGGAG ACAATTTTTC CATGGACCAG TGTCAGGGGG CTGGGAGGCA

TGGTTTTGGG ATGAGTCAAG TACATTACGT TTGTTGTATA CTTTATTTCT ATTATTATTA

FIGURE 16 (49)

TATTGTAATA TATAATGAAA TAATTACACA ACTCACCATA ATGTAGGAAT CAGTGGGGAG

CCCTAAGTTT GTTTTCCTGC AACTAGACAG TCCCATCTGG GGGCAATGGG AGATAGTGAC

AGATCATCAA GCATTAGATT CTCATAAGGA GTGCTCAGCC TAGATCCCCG GCATGTGCAG

TTCACAATAG GATTTGCTCA CCTATGAGAA TCTAATGCCA CTGCTGATCT GACAGGAGGT

GGAGCTCGGG CAGTAATGCG AGGGTTGGGG AGCAGCTGTC AATATAGATG AAGCTTTGCT

CGCTCGCCTG CCACTCACCT CCTGCTGTGT GGTCCACTTC CTAACAGGTC ACAGACTGGT

ACTGGTCCAT GGCCAGGGAG TTGGGACCCT GTCTTAGGGA GTAGGGGTGG AGTTCCCTTC

ACTTCTAGAA GGCCCTGGAT TAGTATCCCA GAGCTGTCAT TACAGAGTAT CACAAACCAG

GTGGCTAAAA ACAGACATGA ATTCTCTCTT ATTTTTGATG GCTTGGAAGT CCAAAGTCAA

GGTGCTGCCA GGGCCATGCT CCCTCTGAAA TGTGTAGGGG AGAATCCTTC CTTCCTCTTT

CTAGCTTCTG GTGGTTTGCT GGCAATCACT GGCATCGCTT GGCTTGCAGC ACTTCAACAT

FIGURE 16 (50)

CTGCCTTTAC TGTCTCATAG TGTTCTCCCC TCATGTCTCC AGGTCTCTCT GTCTCTCTTC

TTTGTATAAG GAAACTAGTC ATATTGGATT AAGGGCCAAC CCTACTCTAG TATGACCTCA

TCTTAAGGTC ACATGCAATG ACTATTCCAG ATAAGGTCAC ATTCTGAAGA ACTGGGAGTT

AGGACTTCAT ATCTTTTGAA GGAACACAGT TCAACCAATA ACAGCCCCTG TACTGTTTTA

CAAATAGGTA TTCCTCTCCT TCCCAAAGTT CTTCATAGCA GAGACAACTT GTACCAAAAG

GCAAAATACC TTATTATGTA ACCTTAACCT AGGATCATAG ATCCCTACTT GTCTGGTGCT

TTTATAAGCC ACAGAACCAC CCGGGAAATC ATTATTAAGA CAAGGAAAGG CCAAGTGCAG

TGGTTCATGC CTGTAATCCC AGCACTTTGG GAAATTGAGG CGAGTGGATC ACCTGAAGTC

AAGAGTTTGA GACCAAACTG ACCAGCATGA CAGAACCCCA TCTTTACTAA AAATACAAAA

ATTAGTTGGG CATGGTGGCA TGTGCCTGTA ATCCCAGCTA CTCAAAAGAC TGAGGCAGGA

AAATCACTTG AACCGAGGAT GCCAAGATAG CAGTGAGCCA ATATCGTGCC ACTGCACTCC

FIGURE 16 (51)

AGTCTGGATG ATAGAGCAAG ATCCTGTCTC AAAAAATTAA TAAATAAATA AAAAGACAAG

GAAAGCCTTT TCCAAGGAGA CCCTTCTGCT TTGCTAGTTC AGAGAACTTC TCTTTGGAGA

AAACAAACAC CCAGTCCATT AGCAGCAACG TCAGGGATTG AATTCTTAGG GCAGCAGGCT

GGGCACAGTG GCTCATGCCT GTAATCCCAG TACTTTGGGA GGCTGAGATG GGTGGATCAC

TTGACATCAG GTGTTCGAGA CCAGCCTGGC CAACATGGTG AAAACTCATC TCTACAAAAA

ATATGAAAAA AAAAAAAAAG CTGGGTGTGT TGGCTTATGC CTGTAGTCTC AGCTACCTGG

GAGGCTGAAG CAGGAGAATC ACTTGAACCC GGGAGTTGGA GGTTGCAGTG AGCTGAGATT

GCCCTACTGT ACTCCAACCT GGGTGACAGA GAGAGACTCC ATCTCAAAAA AATAAAGAAT

TCTTCGGGCA GCAGTCTTTC CTCCACCTCA TAGACCATGG AGGTGAGCCA GCTCTGACAA

ACCATGAGAA CAATGGCAGA GACATACCTG TAACGTAACT GACTGGGGCA AAGACAAAGG

TGAGGAAAAT GACAAGTTTG AGGAACTATG AGACCAGGCA GTGGGGAACA CCACTAGCAG

FIGURE 16 (52)

AAATGATGGA AGTTCTCAAG AATAACAACA GAGAAATAGA CCATGGCCAG AGTCTAGAAC

CCTCCAGGGA AAGGAGATGG GCTCCAGAGG CAGAAGAGGA CGTTGAAGGG AATGGGGAGT

GGGTGAAATA TATAGACGAT GGGGACCACC CAAGAGCAGT CGCTATTGCA AAACTGAGGA

GAAGGAGAGT CTGGAGGGGG TGGTGGGAAG CTGGGTCTCC TAAGGAGGTT TTGACAAAAG

CAGTCATGGA GCGGGCTTAG AAATCACAGT TGGGGACAGG GTAAAGTTCC TCGGGATATA

GAGGATGAGA TTAGAAGAGG TTCCAACTAG GGTAGTGTGG AGAAAAGCAC TATTGACCCA

AAAAGGAAGG AGAATGTGGG TGGAAGTGGC AGAGAAAGAG GGGTTTGAGC AGAGAGTGGT

GATTTTTCTA ATGCAGAGTT GTGGGAGGTG GAGTGCAGGG AGCCAGGCTG GGTGGCTGTG

CTGATGTGAT TAAGCACTTA CTGACTGCCA GGCAATGGGC TAAGTACCTG AGATGCTTTG

TCTGTTATCC CTCCCGAAAC CCCTCTGAGC AGGTGCAGTT ATTATTCTCA CTTCACAGAT

AAGGAAATTG AGGCACAGAG AATTGAGTAA CTTACCCAAG GTGACATAGC TCATATATGG

FIGURE 16 (53)

TAAAGCAGGC TTTGAACTCA GTCTAGCTCC CGAACCTAAG CTTGTAACTA CTATGCTTTT

CCCAAAAAAA GGGGGCTGGC ACAAAAAGAG CTGAGGGGGG CTGGGCATGG TGGCTCATGC

CTGTAATCCC AGCACTTCGG GAGACTGAGG CAGGTGGTTC ACCAGAGGTC AGGAGTTCGA

GACCAGCCTG GTCAACATGG TGAAGCCCTG TCTCTACTAA AAATACAAAA ATTAGCTGGG

TGTGGTGGTG TGCACCTGTA GTCCCAGCTA CTTTGGGAGG CTGAGGCAGG AGAATCGCTT

GAACCCCAGA GGCGGATGTT GTAGTGAGCC AAGATCATGC CACTGGACTC CAGCCTGGGT

GACAGAGTGA GACTCCATCC AAAAAAAAGA AGAGCTGAGG TGATGGCCAC CATCAGCATC

AGCCTGGAAG TTATAGCAGG ATGCTAAGTT TCTCTAAAGC TGTCTTTCTT AGGACTTGAA

AAAGATAACT TGGGTTTGTA TCCCATCTCT GCCATTAGTA GTTTACTGGC TTTGGATAAA

TTACTTAGCC TTACTGAACC AACTTTGGAT TTTTATAGAG ATACTGTAAT GAAAGGAATA

AGGTATCAGT CTTAGCAGAG CATCCAGAGT GTTCCTATTA AAACCTAAAT CATATCCTGT

FIGURE 16 (54)

CATTGCTCTG CCCCAAACCA TTCAATGGCT TCCCAACTCA AAGTTAAAAA CTCATCTTTC

CAGTGGCCTG CAAGAGCCTA TGCTATCCGG TGTCTGACCT CATCTGTTGT TCCTTTCTCC

CTCCCTTTCT TGGCTCCAGA CGCACTCTGG TCTCCTTGCT GTTCCTTGAA TACACCAGGC

ACACTCTTTT CACCTGAAAC ACTTTACCCC AGATATCTTA GCTTACTCTC TGCCTCCCTC

AATTCATTGA TGAAATGTCT CAGTGAAGTC TTCTCTCTCT CCTCTGTAAA AGTATACTCT

CTGTTCCCCT TCTTTACTGT TCTAGCTACT ATTGCTGTGT AACAAATCAC TCCCCAAATT

TAATGAGTGA AAACATCAGC CATCATCTTA TTTCTCACGG TTTCTGAGGG TCAGGAATTC

TGGAAGGGCT CAGCTGGGAG GTTCTGGCTC TATAATCTCT TATGCAGTGA GAGTCAGATG

CTGGCTAAAA CTGAAACAAA GCAGGGTTCT AGTAGCTGAG GGCTGGCTGG GTCTCTCAGA

TATAGTTCAG ATCTCCTCCA GGGGGTCTCT CCACGTGGGC TAGTCTGAAC TTCCTCACAG

CATGGTGGCC TCAGGGCAGT GGACTCTGCA TAGTGGCTGA AGGCTTCGCA GCTGAGTATT

FIGURE 16 (55)

CCAGCAAGCA AAGTGGGAGC TGTATTGCCT CATATGACCC AACCTTGGAA TCCACACAGC

ATCACTTCCG TGTATTCTAC GGGTTGAAAA GTCACAAAAA CCAACCAGTT TCAAGGAGAA

GGAACAGAGA TCACATTTCT CAATTGGAGA AGGGTCAAAG TCACATTGTA ATCAGAGCCT

ATGGGATACG AAGTATTGCG GTCAGGTATG AAAAATTTGA TTTGCTGCAT CTGCTTTACT

TTCTCCACAG CGTTCATGAT CTGCTTCTCA CATGATATTG ACTTACGTCA TTTCTGCATT

TCCTGTCTTC CACACTAAAA TGTCAGCCTG TTTTGTTCAC TGCTGTATCC CCAGAGCCTA

GCACGGAGCC CAGCATGTAG TGGTATCCAA TAAATACTTG TTGCATGAAT GAATTCTGTC

TTTTAATCCT AGCTATAGGT TTCTAAGTTA AATATTACTA TAATCATCTT ACAGACGAGG

GAAATGAGGC TCAAGAAGAT TTGGTAACTT ATGCGGGATC ACTCAGCCAC ATAATGGAAG

AGACAGCATT GAAGTACACA TGCTTGCTCT GTCTGCTCTT CCAAGCTGCT CATCACACAG

CTGCACCTCT GAGGACTTCC CTCCCCAGTC CACCTCCACC CTTACCCAGA GACACACATG

FIGURE 16 (56)

GCCACAATCC ACTAGCAGAC CAAAATTCAA TTTTTCCCCA GTTGGTTGCA CTCAAGCTGA

GAGCAAAGCA ATTGCACTTT AAATCCCCTT ACAGCAGATA TTTCAGAGCA TGTTCGGAAG

AACCCATCAC ACTTGGCTTT TAGATCTTAT TTCTGGTTTG TTACAAAAAC ACAATTAAAT

GAAAGGTTAG GTAGCTTTTG AATGGCCAGC TCAAAGTTTT GGCTTATTTT TGCCTTGCTG

TCTTTATAGG CATTTTACCA ATATTTATCA CTATTTCCCT TAGGGAACCC TTAGATCTGT

GATATTTGAA ATAATAAAGC CTCTCCATTG GCCCTTTAAA AGGTTTGTGG TAAAACCACA

CCATTAACAT TCACAGTTCC TTATTTATGA GGCCTGATTG CACTTATTTC CATATTTCTC

ACTGTTTCTC CGATGAGGAT TTCACATAAT AGTGTTTGAA GGCTAAAGAC TTCAAAGCAG

ATTCTTTACT ATTTTTATCT TGAAAAATAT TCAATATTTG TGTAATTAAA GTGAAGTCTT

CCTAGAGAAA ATGACAACTC AAATAATCTT AAATGTACCT CCAAGAAAAA AGCTGTCAAA

GTGACATTTA GTAGTAGAGT CACATTCTCT AAGGCCTTTG CTTCTCCTTC TGAGTTCTTA

FIGURE 16 (57)

TCATCTTTGA AGGTTATGTC ATGGCTGACT TCAAATCACT TTTAAAATTA TTATGGCCTT

CTTTAAATGT GAGTTCTGAA GGTGAGGGGC TTTATCTTTC TTTTGCTCCA GATTTTTTCT

ACCGCGTCAT TACCAAGCAT CTTAAAACAA AACCTAAAAA CAAAAATCTT CCTTGACCTG

GTTTTTCCCA CTAGCTAACA TCCTATTTTT ATCTTTCCCT TTGCACTAAA GGTTTTTAAA

CGGATCTTTA TACCCTCTGT CTCCATTTTC TCATCTGCTA ACTTATATGG CAAAGATTAC

CACTGCCTTT CAACATAATT GGCCAATCTA CAGAAAGTTT TCAAGTTCTC TTTTTAATTG

ACCACCTCCT GCCTACCTCC CCACCTTTGA CATCTTGCTT CTCACTTGGC ACCTTACCCA

GTGTTCAAGA TTCCCTCCTT TAGGATGTCT TCAGAGCAGC TACACAGTTG GTACTATAAT

TTATACATCC TTGTACACAG GGCTTGCTGG GATATTGATG GAGAGAAGGA GGAAACTGGA

AGTAGTTCAG GCCAGAGCTA GGGAAATTGA CCCATCTCCA GGTCTCAGGT CTGCAAGGGG

AGCTCACAGC TTAACACATG GAGTCTAGAA ACTTGTGCTG GACCTTGACC AACACCAGCC

FIGURE 16 (58)

CATGGAGTCC AATACAGTGC TCAATAGGGA TTTCCAGGAA ATTGCTATAT TTATTCAAAG

AGAACTTACC AAGTGTCAGC TACGTGTTGG GCATTGTGTT AGGCACAGGG ACCACAAAGA

TAAGACATTG TAGCTTTCCT TAAGTTGCTC ACTGAGTAAA TAGAGAGACA GAAAGGTAAA

CAGGTAAGTG CAAAAATACA TACAATTCTG CAATAGTGTT CATAGTGGCT ATGGAGAGAA

CGCTCACTAA CTTTGTTTAA ACAGTTGTTC TTTCAAGGAT TTGACATGGA TTTGATTGGA

AAAGCATGAT ACCATTTTTT GCAATTAAAC ACAGGAATAC ATAAATAAAA TGCATCAGTA

TTTTTTACAA ATAGCTACTA AGAGCTACTA GAAAACCTGG GAATTCTTAA AACCTTACCA

TGCTACTTGC TCTAAAATAT TTTATTTTAT GTTATTTTGT ACATTTCTTT ACCTACACAA

ACACCACTGT TTTCTTCATT TCTTAGTCTA TTTAAACCTC ACACCCTTTC AGCATCTCTT

AATTATTTAC TACCATCTGT TAGTTCTCCT GTCCTGAATG AAACAAAAAT GGCAGAATGT

AAAACGAGGG CGAACAGATT TTTGACAGGA AGTATTCAGA GGTAGAAGGA AATAGTCAAG

FIGURE 16 (59)

ACACATATGA TAAACGAAAA CAATAATAAC TTTATACATA ACAACTTATA GACACATTTA

AAAAGTTTAA GATCTCAAGA GCTATGTCTG AATAGATAGA AGTAAAAACT CTATTAAGTA

ATTAGGAAAA TAACAAGAAC AGTGAATTTC TTAATGAATG GCATGTAATC AAAACTGTAC

TTATCGTCTA ATTCATAATC TTGAATGTTT TTATTTTATT TATTTATTTT TTTATTTTTT

GAGACAGAGT CTTGCTCTGT CACCCAGGCT AGAGTACAGT GGCGTGATCT CAGCTCACTG

CAACCTCCAC CTCCCAGGTT CAAGCGATTC TGCTGCCTCA GCCTCCTGAG TAGCTGGGAT

TACAGAGGCC TGCCACTGCA CCCGGCTAAT TTCTGTATTT TTAGTAGAGA TGGGGTTTCA

CCATCTTGGC CAGGCTGGTC TTGAACTCCT GACCTCATGA TCCACCAGCC TTGGCCTCCC

AAAGTGCTGG GATTACAGGC GTGAGCCACC ACGCCTGGTC GAATGTTTTT ATTATTTGAA

GAGACAACAT GGGCCTTAAA TCTGTCTTCT ATTTGACAGA CTTTGATGGA GTCAAATCCC

AATGCTGCCA CTTACTGAAC GGCCTTAAAT GACTTAGTCT CTCTCAGCTG TCTTTCTGCA

FIGURE 16 (60)

TATGTAAGGT GGAATAATGA TGGCTTCAAG GAGGAATAAA CCTATGAAAA GTGTTGAGGA

TAGTGTCTGA TATGAAATAA GGATTCAACA AGTAGTAGCT GCTATTGAAG ATTTAAGAGT

TATTTATTAC AACTATTTAA TAAAATTTTA AAAACTAATA CACTTAAATT ATTAAAGAGC

TTTGAAATGG GCCAGGCGCA GTAGCTCCTG CCTGTAATCC CAACACTTTG GGAGGCCAAG

GTGGGCGGAT CACCTGAGGT CAGGAGTTTA AGACCAGCCT GGCCAACATG GTGAAACCCT

GTCTCTACTA AAAACGCAAA AATTAGCCAG GTGTGGTGGC ATGCACCTGT AGTCCCAACT

ACTCAGGAGG TTGAGGGAGG AGAATTGCTT GAACCTAGGA GCTGGAGGTT GCAGTGACCC

GAGATGTCAC TGCACTCCAG CCTGGCAACA GAGCAAGACT CCATAAAGAC AACAAAAGCT

TTGAAATTGT GTAAATGAGT TGTACCTATC TTCATTTAAG AAATTCATCT TTGTTCATCT

ATTTTTACTT GACATGAGAG CTTCCAGCAA TTTTTAATTA AGCCCTCACA GATTTTATGT

CACTGGCTAT GTGATAAACA AATTATTTGC TAAAATAATA TTCTTGCTTC TTTTTTAAGG

FIGURE 16 (61)

AATTGTCTCC CTAGAAACGG TTTGTACCAA ACAATACACT GACTTTACAC AAAATCAGAT

CTGATTGGCA ACAGTTGCAG ATGTTTTCAA AGGATTTTCA TTTGAGAAGG GGCCCATTTG

GGTTATTTAG ATTCTAAGAA CTGAAACTGC TTTGTTCTGT TTTTCTGGCT TCTGGGAGAG

GAGGAGACAT GAATTCAGTT AGCACCTTGG TATTTTCTTT ATCCTTCATT TCAATACAGA

AGATGCTTCA TATGCACAGT GGTGTCAGGT CACATCAAAA GAAAGAGAAA CAGTTTCTTG

GTTTTTAATT TTCAACCGGA AAGGAAAGGC ACCCATTTTG TTCCGCTCTA ATTAGCCAGT

GCATGACTTA GAGAGCAGGC AGATGCTTTG AAGGCGTGGT AACACAGGTC TTCATTAATC

TCCACGCAGG ACTTGCACTT CTACTATGCC TAGGCTGAAG AAAATGGCTC AGGAAGATGA

ACAATCTCAC AGAGCCCTAA CTAACTGAAG CCAGGTGTTA TAAAGCACAA GTCAAGAGGG

TGAGAAACTA ACGTTCTTGA AATCTCCCAC TTCTTTCTAC GTCAGAAGAG CCAAGCTGAT

TATTTTAGTT GGAATTTAGA AATTTTTAAA AATTATTCTA AAGTCATGAA CAAGCCTAAT

FIGURE 16 (62)

TATAAAGATA GTTGCTGTGA AGGTGCTGAA ATAACTCGAT TTTACCAACC CCCTCTTCTG

GAGGAAGCCA GAATGGAATC CTGTAGAATG TTCACTCTAC CAACGAACTC TTGTTTTTCT

AATGAGGAAA CAGAGGCCCA CAGTAGTAAA CTATCTTAAC CAAGACAAAA TGACTAGTGC

TCTGGTCCTT TTATTAAGCA CTAAAATTTT GATCCAATAA TAAATCTGTC CAGTAGAAGG

AGTTTCCCTA ATGTACTGGT TCTAACTTGT TCCCTTCAAG GGGCCAGTGT CCCGTACACA

TAGCTAAATG GGACTTCTCT TCAACTACCA TTACCCAGAG GGCAGAACCT AAAATGCTGT

GAATGACATT CTGCTGTTCA CATCTCAGCA GCAGTGTTGC ATTTGAGCTT CTGCAGGGCC

ACCCAGGACC TATATCTGCT CAGATGTTTA ACTCATCTAA TTCAGTGAAC ACTTCATTCT

AGTTAACTGA ACATCTACTT TGTACAAGGC ACTACAGCGG TTCAGAGATG AATAAAATCA

TGAGATTCCA CTGTCTCCTA TAAACCATCA CTTTGGGAAA TTTTAGAAAT GTGGGTAAGC

TCCAGGGCTT CCTGCAGCGT AGAAGTCACA AACTCAAATG CCTGCAGAGG CCCAGCTGAC

FIGURE 16 (63)

AACATAAGTA AATGATTCTG GCTGGGCGGA AAACAATTAC GGGTGGGTGG GTTTCCAGCT

GGGGAGTGCA CGCCTGTGTT AAAGGACA

GCTGCTACTC ATTTCCAGCC AACTGTGTTC CCATGTAGAA CTGCGGCCCA GTGTAGCCAG

TACCGAAGAT TTCTCAGAAA AAGCCGGAGA TCTCAATGTT AGTGTAAAAT CTCTCAAATT

TCCAAGAGGA TTATATGGGG CAAAGGTTCT CAGATCAGTT TGCAGTCTCT TACTTAGCCC

ATGTGCAGAG CAGTCGTAGA GGGTAGCATG CAGTGTCCTA CATAATAATT CTTTTTTATT

TTATTTTATG CCTTCCTCCT TCCTGTCTCT CTTTAACCTT TCTTCTTCCC TCAGGCTGGC

TTCTTCCCTC AGCCTCGTCC GACCCCAGCC TGGGTTCAAT GAACATTCGG TAAAGGAACA

CGGAATGTCA AGCGCATTAG AGACAACCTT GAGACACATT CCTCTTGCGG TAAGCACTTC

ACTGTAGATT TTTAATTTTA AACAAGACAA TGTTTACGAC TTGCTTCTTT CAGGGAAGAG

CGATATCAAT TTTAGTGAAC ACTTCAAGGC TGAGATACGC TAGGAGAGTC GTGTGGTGTT

FIGURE 16 (64)

GCACAGCAAA GAATTCCACT TTGAAGCGAG TGGGAAAAAA AGCATCAAAT GCCACATGTA

ACTCACCGCC TGAAGGGTTA CATTGGTATG AAACCTGGGT TTAAAAAGGG ACCGAATAGA

CTAGCCATTA AAAGACCTGC GTACAACCTC TCTCTCTCTC TTTGAGAGAT AATGTATCTG

GACAATAAAC ATGAACAGAG TGGAGTCTAT CCTGTTTAAA ACATTGCCTA CTGTACAGGC

ACCAGGAGCT GAAGGGTCAG AATATTAGCA GTGGGAGCTT GATTAGAAGT TGATGAGAGA

TGGGTAGTAG GAGGAAAGAG TGAGATAGAG GAAGAGGACA TGGGGGTTAC CCGTAAGTGG

AGAGTAGAAA AGTAGAATCA GCTGGCCATC AAAGGGCGTG GGACTGAGGA ACAGTATGGC

ATGTATTAAA TATACTAAGC GCTGACATTG GAGGAGAACT AGGAAGGTAA ATGAAATCAA

TAGGGGATGA TGGAGAATAG TTAGGTGTGC AGGGATTAGG GTTATGATAG AAATACATGT

GAATACATGC AGTATTGTCC TGGAAAATGG TTAACAGTTG GTTCTCCTGG GGGGTGAGGG

GAAGCCCTGA TTTGTAATAT TTGCCTATTT CTGTGGTGCA AATACTCCCA CCATGACCAG

FIGURE 16 (65)

TTTCAAGCTA TGAATGTGAA TCACAAAAGC AGGTTGGGAG GAGATGCGCA CATTTGTTCC

CCGGCAAGGT GGAAGGTAAG GAAGGTGAAA TCAACAAGGT CAAAGAAAAC TCAAGATTTC

GAGGTGCCTC AGGTCTGAGG GGCAATGAAG TCTAGGAATG GCTGTGCTGA GGTAGCTGAA

ATAGAAGTGA CTGCAGAGGT CATGAAGCTG AAGAGGTGAA AACAGAAATT AGAAAGGCAA

ACCCCCACCG CCCAACCCCC ACCCCTGCAG CCAGTTTCTG AGGGTGACAA TAGAGGAAAG

GGTGGAGATG GAGTTCAGGT CCAGAAGCCA TAGAAGCGAG TGTGACATTG TGCTCAAGGT

CAGCACATGT CAGTGTGGGG TGTCACATGC TGTTGTGAAC CATCATTTAT CACCAATTAT

GGAAGACCTC CTATGGGCAT CTTGCCATAT GCATTATAAA GATGTGTAAG AAGACATTTC

CCTCCACTTG GTGAGGAGAA TTAGGGCTGT ACACAGATAC TGTAGAGTGC CATGTGCCTG

GTACAGATAA GGTGTGTTAG AGGTTAAAAG ATGAGGCTCT TAATATTAAT GATAGATCCC

ACTTACCTGA GTCTGACTTA CAATGTGCCT AGCATTAAGT GTTTTACCTG CATTCCCTTT

FIGURE 16 (66)

GACCTTCAGA ACAACCCATT TTACAGATAG GGAAATTGGG TCAGAAAGTT TCAGTAACTT

ATCCAAGGTC ACACAATTGG CAAGTGCCAG AGCTGAGCCA GGAACTGAGG TCCTTCTAAC

ACCAAACAGC TTGTCTCCCC AATCACTGTG CTATTTTCCC TCCCCCAGAA GATAATACTC

TGATGGAAAT GAAGGATAGT GTAATAGGAG ATTCGGTGTT CCTTTTTTTA AAAAAAATTC

AGCTTGCATA TTCCTAAAGA GTCAATTCAT GTTTAAAAAA AATTTCCCTT GTGCTTGCAT

GTGACATGTA TTTTTAGGAT CTGCTGTTAG CAAGTGTATT TTTGTGTGAT TGAGTGGGAG

AGTGGGAAAA GTTTTGCAGA GCTGTTGAAG CCAGAATGCA GGGGGGCTGC GCAGCAGAGA

CTGTAAAATC TCTGCCATCT CAGGTCTTGG AACAAGCACA AAGAGATGTG TTCTCGATTT

ATTATTCTAT GTACATCCCC AGATGAATGA CTAGTTAAAG GTATTGTTAA AGCATTTTAA

ATGACCCACT TCCAGCAGCG AACAAAATCA CTTGCTGTGC CAAGCCAACT GGCATTTCTG

AGATGATAAA ACCACAAAGT GAGGAAAACG TTAAAACTGC TAAAGCAAAA ATGATACACA

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233/285	244/285
234/285	245/285
235/285	246/285
236/285	247/285
237/285	248/285
238/285	249/285

FIGURE 16 (67)

ATAATGGAGA AGGAGAAAAA TTGAGCTTTA TTGTCTGCCT AGGCAGATGG CTGACCACTA

GGTGGGCTCG GCGTCACGTC CAGGGTAATT GGTTGCTGGG GTGTTTCTGG CGAGGAAGAT

TCACGCTTCA GCTCGGTCCA CAAGATCCTG GCTCATTCTT TCCTAGATTC CATTTTCTGC

CTCCTCTCCA TGACTGGGTC TGATGGTTGA TCCAAACGGG CAATTGAAAT CAGAAGGTTA

CCTTTACCTT AAAATGCTTT TCTGGAAATA AAAGGACATG AAAAGTAACT AAGGACCGGA

TTTCCTAGCC GTCTTTCTCT CCTGCATGCG CAATTTATCC CCAGATATAA AATTGCCTGC

TTTGATAATT ATACCCTCTA AATGAGGGGC AAGTGGCTAA TTATGCCCAC ATGTGGCCGA

TTGCACTCCC CATTAGCCAA TTATGTGCTC AATTATTTGT GCACATGAAT AATTGCACTC

ATGGAAAATA GCGGCCCTCC TTTCAAATCC TCGTGCTTGG AGTGGCTGAT GGAGTAATTG

TCACACTGGA AATGCACTTG GTGGGGAGGG AAAGAGTATC AGATACCAGG AAACGCATAA

GTGACCAGAG CTCGCAGATG TTCACTGCCA CAAATGGCCT TAGGAGCCAG AGAGAGCGGG

FIGURE 16 (68)

AAGGACCACA GGATGGAACG GGCCAGCCTG TGAGTTAGGA AGCCTGCTTC TGAAGTTGCC

TGGGCAGCTC ATGTGCGGTG ACCTTGGGCA AGTCATTAAC TTTCCTTCAG GTCTAACTGG

TTCTGCATAC ACAATGAGGA TGGTAATAAC GCCCAATTCC CATCACTATC GTGGGATGGA

TCAGACTATT TAAAAGGATT TACAATCTGC TTGGGTAAAA GCTTTACATA AATATGAGGC

ATTATCATGT CGCTTGGTAC ATCTCCAATT ATGAAGGAAG GGTAATGACC CTCCACAGCA

ATGCAGGACT CCTGGTTTGG AGGGAGGGAA AGTTTGAGAA GGACAGGAAG CTTGTTGCCC

CAGCACTGAT GTTTCTACTG AGGTACCAGA AAATGTCATG TGGTCATACA GAATTCATTT

ATTCATTCAA CAAACATCTG TCAATTGTTA CACTGTCCTG AGAATTTGGA AAAATGATGA

AAGACTCAGT CCTGCCTTAG GAGGTCACTG GCACATTGGC CCGGGCCCCT GTTTTGGGCC

TTTTACTCTG ACCTGTGCTG ATTTGCAAAT AGTGGGAAAT TTTATCTCAA GTCTAGGAAA

TCTGGCATGC ATTTTCACGG TTTGATTGCC AGGTACATTC GATGGCAATG AGTCTTATAA

FIGURE 16 (69)

TGTTTGGTTA CCTTCATTTA CCTAAAAACT GTGGTTGTTG CTGTGGTTGT TGTTTTTGTT

GTTTTTGAGA CGGAGTCTTG CTCTGTCATC CAGGCTGGAG TGCAGTGGCA TGATCTCCGG

TCACTGCAAA CTCCACCTCC CAGGTTCAAG CGATTCTCAT GCCTCAGCCC CCTCAGTAGC

TGGATTACAG GCGCGCACCA CCATGCCCGG CTAATTTTTG TATTTTTAGT GGAGACAGAG

TTTCACCATG TTTGGCCAGG CTGGTCTCGA ACTCCTGATC TCTGGTGATC CGCCTGCCTC

GGCCTCCCAA AGTGCTGTGA TTACAGGCGT GAGCCACTGT GCCCAGCCAG AACTGTGGTT

TTAATGACAA TGCTAAAAAG TGGTATATGT CACAGTGTCG GGTGGGGCTA AGAGGCACAT

TGCTGCAGTG ATCCATCATT CATTTCCCAC CATTCTCGCC TGGATTAGCG CAGCAGCTCC

CAGAGAGGCA CCTCACTTTG ACCTTCTTCC TCAAAGACAT TCTCTGTGAC CTGCCTGGCC

CTTATTACCT CTCTAGCTTT GCCACTTCCC TATGTCTCCA TCTCCCCTCT CACACGTAGT

AAGAAAGAGA CTCTACCTCC ATGGAAGTTA AGGAGAGGTT TCACAGAGGC AGGATTGCTT

FIGURE 16 (70)

ATTAGTCTTC AAAGATGAGG TATTTGCTAA ATGAATGAGA CAAAGGGATT GGGGCCACAT

TACAGGAAAT TGAGGTATGT AATAGCCTGG TGCAGGTTAA GAGTGTGGAC TCTGAAACCA

GACTCAGCCT GGAATTGAAT CCTGGCTGTG TGATGTTGGG CCAGTGACTT AACCTCTCTG

TGCTTTTATT CACTCTTCTA TAAAATGGGG ATTATAATAA ACCTACCTTA TAAGGTTATT

ATAAGAGTCA GTAAATATAA AAATAGAAGT TTTTGGATGA TGACTAGCAC AGAGTAAACA

CTTGTTTGCC ATTATTTTTA TTACTTGACT AAAAATATAC CAAAAAGACC ATCCAAGAAA

AGCCTTTAAG CTGCTAGTGC AGAAAGATTC CCCTTGTGTT TGTGTGCTGG GGGGTCAGTG

GTGCCTGTGG CCCACTGGAG AGGAGACAGC TATGGCTGGA GTGATTCTCA AACTTCAGAA

TGTCTAAAAT CATCACATGG ACAACTTATT AAGGAAAGCA AATGCCTGGG CTCCATCCTC

AGAGAGTCTC ATTCACTGGG TCAGGATAGA GCCCAGGAAT CTTTACCTTA AAGAACCATC

CCACCTCCCA CCTCATATGA TCCTTATGCA GGTGATCTGG GGGCCCACAC TTTGAGAAAT

FIGURE 16 (71)

AGACTCAGGT CAAAGTGGGC TCTAACTGCA TCTCATTTCT TACCTGGCAT ATCTAATAGT

AGAGAAGAAG ACAATGCTAA GATTTTTGTT GGAGATCTTT TGCTGGGATT GCTGCTTCAT

TCATTCACTC ATTTATTTAT TTATTTATTT ATTTTGAAAC AGAGTCTCAC TTTGTCACCC

AGGCTGGAGG GCAGTGGCAC AATCTGAGCT CACTGCAGCC TCAGGCTCCT GGGTTCAATC

GATTCTCTTG CCTCAGCCTC CCGAGTAGCT GGGATTACAG TCATGCACCA CCACGCCCAA

CTAATTCTTG TATTTTTAGT AGTGACAGCG TTTCACCATG TTAGCTAGAC TGGTCTCGAA

CTCCTGACAT CAGGTAATCT GCCTGCCTCG GCCTCTCAAA ATTAGTAGCT GCAATTACAC

GTGTGAGCTG CCGTGCCTGG CCTGCTGTTT CTTTTAGTTG GGCCTCTTCT GTAATAGAGT

GTGAGAATTC TGACTTGCTG CAACAGTCTG CTTTGAAGCA GGGCTGTGTT TACACTGGTC

AGATGTGGAA TTGTGGGGCA CACTTAGCAG CTTCCTTCTC TAATTTTTCT GTATTTTCAG

GAGAACAATT TTAAAAAATT TAATAAAAAT GCCTTAAAAA TTAACATTAT TATAAGATGA

FIGURE 16 (72)

ATCCCATTTT TCTAATCTTG TAAATTAAAA ACAATCATAA GCATATGAGC ACCTGCACTT

AGGGAATCAA GGTGGCAAAG CTAAACACTT CCAGCTCTAG GTGATTCGCG GCAATACAAA

TGGAGCTGGA CTTTGGCCAC AGTGCAAAAA TATTGATCTG TTGTTAGATG CTCTGAAGTT

TCCACAAAGA ATTGGTTCTG CCTGCTGTGC TTCAGTGCTT AAGGGAAGTG GTTCCTCAAA

ATGTTAGTTT TTAAGCCCAG CTTTCTTAAA TAGGAAGATT CTAATAGTAG CAAAAATATA

AACTGCTTCT AGGTTTAAAA AGGACCAGCA CACAATGGTT ATCACACACC TTTCTCCTCA

GGTGATGAGT GGATGAGTGG CCTGGTGTAT TTCATAACAT CTCCCAGGGT CCAAATGCTA

AAGCAATTGC TGAAAAGATA CCATGTGTAC CGGAACCTTG CAGAGGTATT TTGTTGGCAT

AAAAAGAAAT ATTGATCATC TATAGTAAAA ATGGTTCTAC TTTAATACTA CTGAGAAAAG

ATTTTCTTTT CCCAGATCTA CATCCTGAAT CTTCATGAAG ACAAGATCCC CTAAACTTCC

ACTAACACCA TAATGTGTGC TGTCCTTTGT AATGTAGTCC ACAGATCTCA TAAACTGTCA

FIGURE 16 (73)

GAAATAGCAG AGATTGTAAG GTCATCCACT TCCCCTGTAA GGCCTGCGTC CCTCACTTAC

ATCCCTAATA ACGTCCTCTA ACCTCTGCTG GAGGGCAGAT TTAGCTGCCA GCTGGGAAGA

GCTCTGCCCT AGTCAACATT TTTATCTGTG GCTTTCAGAT GAGAACACTG GATGCTTATC

TGAAAAAAGC TCCTCAGGCT GGAGGGAGGG ATTGGCTCTA ACAAGATGCA ATGTGATAAG

AATAAAAGCG AAGCCAAACT CTAGGCCCAA AGGCTCTAGC AACACACTTT TGAGAACCTT

GGAGACGAGT TTTGGCTGAT GCGAGCTTCT CCGCCTGCTA AAGTAGCCCA TTCCATTTGG

ACGGCTCTAG AGGCTGGCAT GTTCTTCTCC ACGTTGTGTT AATGTACTCC AGTTTCTTCC

TGCCATGAAC TGGCATGCCC TGGCTCCTCC TACCTTCCCC ACTTTAAGTC TTCCCTCCCT

CCTTCTGACC TTCCCATTCC AGCCACACTG GCCTTTTGTC TGGTCCTAAC AAACCATGCC

TTTCCTGCCT CCAAGCCCTA CACCTGCTAT CCATCCCTCT GTCTGAGAGA CACTCCCACC

CCTTCACAAA GCCTGTTTCT CATCCTTCCA GTTCAGATGT CTTCTCAGCT TGCCTCAACT

FIGURE 16 (74)

GACCTCTTTC AGCTATTCTC ACTCTTTGTA CTCTGTTCAT TTCCTTCCTG GCAGTCACCA
TAATTTATCT TTATTTGAAT CAATTTCTTA GTTGTATTAT TTAGTTATTT GCACACTCTG
TCTCTCTGTG CCTTTCTTAT TCACTGCAGG CTTTCTTATG TAAGTAATTT ATTTACTTAA
ATTTTTAAAA ATAATTTCAA CTTTTGGCCG GGCACAGTGG CTCACGCCTG TAATCCCAGC
ACTTTGGGAG GCCGAGGTGG GTAGATCAGC TGAGGTCAGG AGTTCGAGAC CAGCCTGGCC
AACATGGTGA AATCCCATCT CTATTTAAAA TACAAAAACT AGCCGGGCGT GGTGGTATGC
ACCTGTAATC CCAGCTACTC GGGAGGTTGA GGGAGGAGAA TCACTTGAAC CGGGGAGGTG
GAGGTTGCAG TGAGCTGAGA TCACGCCATT GCACTCCAGC CTGGGGCACG AGAGTGAGAC
TTCATCTCAA AAAAACAAAA AACAAAAAAC CCCTGCTTTT CAGAGGGGCT GAACTAATTT
ACATTCTCAC CAATAGTGTA TAAGCATTCC CCTTTCTCTA CAGCCTCACT AGCATTTACT
TTTTTAAAAA ACTTTTTAAT AATAGCCATT CTGACTGGTA TGAGATGGTA TCTCCTTGTG

FIGURE 16 (75)

GTTTTCACTT GCAATTCTCT GATGATTAGT GATATTGAGC ATTGTTTTAT GTTTGTTGGC

TGTTCGTATG TCTTCTTTTG AGAAGTGTCT TTTCATATAT TCTGCCCATT TTTTGAATGG

AGTTGTTTTG TGCTTGTTGA ATTAAGTTCC TTATAGATTC TAGATATTAG ACTTTTGTTG

GATGCATAGT TTGTGAATAT TTTCTCCCAT CCTATAGTTC TGTTTACTCT GTTGATAGTT

CCTGTTTTGT TATGTTTTGT TTTTTTGCTG TACAGAAGCT GTTTAATCTA ATTGGTCCCA

CTTGTCAATT TTTGTTTTTG TTGCAATGGC TTTTGAATTT TAATAATAAA TTCTTTCCTA

AGGCTGATGC CCAGAACAGC ATTTTCTAGG TTTTCTTCTA GGATTCTTAT AGTTCAAAGT

CTTATATTTA AGCTTTTAAT CCACCTCAAG TTAATTTTTA TATATAGTGA AATGCAGGGG

TCCTGTTTCA TTCTTTTGCA TGTGGCCAGC CAGCAATCCC AGAACCATTT ATTGAATAAG

GAATCTTTTC CTCATTGCTT ATTTTGTCAA CTTTGTCAAA GATCGGATGA CTGTAGGAGT

GTGGCTTTTT CTGGGTTATC TACTCTGTTA CATTGGTCTA TGTGTCTGTT TTTGTATCAG

FIGURE 16 (76)

TATCATGCTG TTTTTGTTAC TATGGTCTCA TAACATAGTT TAAAGTTGGA TAATGTTATG

CCTCTGCTTT GCTGTTTTTG CTTAAGATTG CTTTGGCTAT TGAGGCTCTT TTTTCACTTC

ATATGAATTT TAGAATAGTT TTTTCTAATT CTTTGAAAAA TGACCTTGGC AGTTTGATAG

GAATAGCATT GAATCTATAG ATTGCTTTGG GCAGTATGCT ATTTTAATGA TATTGATTCT

TCCTATCCAT GAGCATGGAA TATTTTTCCA TTTGTTTGTG TCATCTACTA TTTCCTTTAG

CAATGTTTTT TAGTTTTCCT TGTAGAGATC CTCCTAGGTA TTTCATTTTT TATGTGACTA

TTTTAAATGG GATTGCATTC TTCATGTGGC TCTCAGCTTG AATGTTATTG GTGTATAGAA

ATGCTACAGA GTTTTGTACA CTGATTCTGT ATCCTGAAAC CTTACTGAAG TCATTTATCA

GTTCTAGGAG CCTTTGGCAA AGTCTGTAGT GTTTTCTAGG TATAGAATCA TATCATTAGC

AAAGAAAGAT AGTTTGACTT CTTCTTTTCC TATTTGAATG CCTTTTATTT CTTTCCCTTG

TCTGATTGCT CTTCCAGTAC TACGTTGAAT AGGAGTGCTG AGAGTGAGCA TCCTTGTCTT

FIGURE 16 (77)

GTTCCACCTC TCAAGGGAAA TGGTTCCAGC TTTTGCCCAT TCAATATGAT GTTGGCCATG

GGTTTGTCAC AGATGGCTCT TATTATTTTG AGGTGTATTC CTTTGATGCC TAGTTTGTCA

AAGGCCTTTA TCATGAAGGG ATGTTGGATT TTATTGAAAG CTTTTTCTGG GTCTTATTTG

GTGAATTGCA TTTATTGAAT TGTGCATGTT GAGCCAAACT TCCATCCCAG GGATTAAACC

TACTTAATCA TGGTGTTAAC TTTTTGATGT GCTGCTGGAT TTGGTTTGCT AATTTTTTTT

TTTTTTTTAA AATGGATTCT CCCTCTGTCC CCCAGGCTGG ATTGCAGTGG TGTGATCTTG

GCTCACTGCA AGCTCCACCT CCCGATTTCA TGCCATTCTC CTGCCTCAGC CTCCCGATTA

GCTGGGACTA CAGGCACCCG CTACCATACC CAGCTAATTT TTGTATTTTT TAGTAAAAAC

AGGATTTCAC CATGTTAGCC AGGATGGTCT TGATCTCCTG ACCTCGTGAT CTGCCTGCCT

CAGCCTCCCA AAGTGGCTAG TATTTTTTTA ATTACTATTT TTTCTCACCC TTGCTGCCAT

CTTATGATTT TCTAGTATTT TGTTGAAGAT TTTTGCATCT ATTTTCATCA GGGATATTGG

FIGURE 16 (78)

CCTGTAATTT TCTTTTTTCA TTTCATCTTT ACCACATTTT TGTATCAGGT TCATACTGGC

TTCATAGAAT GAGTTCAGGA ATGGTCCCTC CTCCTCGAAT TTTCTCTGTA GAATTAGTAC

CAGCTCTTTG TGTGTCTGGG AGAAGTTGTA TGCCAATAAT TTAAATGCAG TTAATATTTA

CTGGACAATT TCCTCCAGAT AATTGTATAT GATTTTTGGT CCACCCTGAG TTGATACATG

TATTTTAATT GTATCATGGT ATGAAAAGAG CAAGAGTATT TGGTCACCTA GTCTTGCCTA

TAGATGTGCC TAATGATTCA AAGTAGATAT TTTGGGAGCC TAACAGGTGC CGTGACTAGG

CAGTTTTGTT TTTTTTTTTT TTTGAGACAG AGTCTCGTTA TGCTGCCCAG GCTGGAGTGC

AGTGGCATGA TCTCGGCTCA CTGCAACATC CGCCTCCTGG GTTCAAGCAA TTATACTGCC

TCAGCCTCCC CAGTAGCTGG GACTACAGGC TCACGCCACC ACGCCTGGCT AATTTTTGTA

TTTTTAGTAG AGATGGGGTT TCACCATATT GGCCAGGCTG GTGTTGAACT CCTGGCCTCA

TGATCCACCC GCCTCGGCCT CCCAATGTGC TGGGCTTACA GGCGTGAGCC ACCGCACCCG

FIGURE 16 (79)

GAGATTAGGC AATTTTATAT TCCCAAATAT CCAACTCTTC TGACCCGCTT TCTCAGCCTG

GGTGTATCAG GCACAAGGCC TGTTCAGATT ATGTGGTCTC TGAAGATATG GCTCTCCAGG

GTTGACAATG TGGATAAGGA TTCACCTGGT TTAGGATTTA CACATTCGCC TTGAATGTCT

GTTGCATCAA GTAGACAGTC CATCCCAACT TGGCCATTTG GTCAGAGCTG TAAGGAGACA

AGGAGGTGGG CAGCCGCTGC TGTGAACTGC TTGGACAAAG ACTGCCAAAT AGCTATCAGA

CAGTGTTAAC AACAGCTGAT TTAGGTTTGA AGGGGGCAGT CTCTTGGGCC ACTTACTATG

CTGCATCATC CTCTTTGGAA AATGCTCTTC AGGTAACTGC CTAACAGACT GAGAAAATAA

AATGCTCACA GAGAAAAAAG ACCCGGAAAG TCTGACTTCT CAGAGCTCAG TGTTTAGGTG

CAGAACTGGA TTGTGAAAGG ATTTTTAAAT TTTTTATATT CATTGCAGGG AACATTCATT

TATTCCATCC TTCTCCACTC CCACCTGTCT GTCGTTGTCT TTGTCTCTGT CTCCCCACCT

CTCTCTCTAG ACACACACAC ACACACACAC ACACACACAC ACACACACAC ACACACACAC

FIGURE 16 (80)

ACACACACAC ACACACACAC ACACACACCC CTATTCATTG CCAACAGTAA TAGAGTTGCT

TCTTTACTTC TTGGAGAGAA AAGCCTCAAT CTGAGGAAGC TGTGCTGACT AGCCTTGCTC

TTAATCATGG AGACAATGCT TTATGCCTTT ATCTTTGCAC AGCTGAAAGC CATGGCAGAA

GCAGTCCTCT AAACGAAATA AAATAGAAAG GTTCCTGCTA AGCCCTGGCA AATGCAGCCT

TCTATCCCTC CCCCAACACT CACAGCTTCT GAGCAAGATG TAGCTGCCTT CCAGGAGGCT

GGGTGATGGG CAATAATGAG CAGAGCCACG TGAAGGAAAG ATGGGTGAAG AAATGTGTGT

GGAGGTCATG CTGGCTGCAC TGACCATGAA ACAAAGGATC TACCCCTCTA GTAACTGCCC

TACTCCTTTG GTAACTGTTC TGAAATTATA ACTTGCCAGA AGTTCAGAAG GACCTAGTGC

AGGTATTAGA GGAAATTCGT AAGATTGAGC CATTTATTCC TGCACAGATA CATAATAATG

GACACGGGCC ATGGTGGCCA GCATTCTTGC TCTTGACAAT GGTGAAGGGA AGGGTTGTAG

GTCATGGCTA TGCTCTCAGA ATTATAATGG AAAGAAACAG CTCCTGAGTG TTTACTATGA

FIGURE 16 (81)

GCCAAGGGCT GTGCTAAACA CTTTACCATA TGATGACATC TTTTTCTCAC AGGTATCAAA

AAACAATAGG ACATACCGGA TAGCTACAAT CTTTGGGCCC CTGCAAACAC AATAATGTGT

ATTCTCTTCT TCAAATCCTA CATATTGCTA CAAACTGTAT CCCTGAGGCA TATTCATTGT

AAAATAAAAA CATATAAAGT ACTACTTTTG TTTTTTGAGA TGGAGTCTCG CTCTGTCACC

CAGACTGGAG TGCAATAGCA TGATCGTGGC TCACTGCAAC CCCCTGCTCC TGGGCTCAAG

TGATTCTCCT GACTCAGCCT CTCAAGTAGC TGGGATTACA GGCGCACGCC CCCATGCCTG

GCTAATTTTT GTACTTTTAA TAGAGACCAG GTTTCACCAT GTTGGCCAGG CTGGTCTCAA

ACTCCTGACC TCAAGTGATC CACCTGCCTC GGCCTTCCAA AGTGCTGGCA TTACAGATGT

GAGCCACTGC ACCCGGCCCA TATAAAGTAC TACTAATGTA ACAGGGTGCT AGTCCAGACA

GTGACCACAC GTGGTGTTCA TTGAAGGCTG GACTAACAAC TCCAGCCTCT CCGCCATCAC

FIGURE 16 (82)

CTGCTCTTTG TTGTATACAT GTTAGATGAT CAGGCCTCAA GAAAAGTATA AAGAGATCTT

TGTGCTCTCT GGGACTCAAA AAGCTGCACT CTTTGGGGGA AGGATAGCCA GGTAAAAGTG

GCCCAGGTAA AGAGGGCCTG GTACACCTGG TTCTGCAAGA TGGTAGACAC AAAAATGAGA

GCCACATTTG GAGCTTATGT GCCCCTAACT CTGTACATAA CCTGCAAGAT CTAATTACTA

ACAACTGGAA TCTTGGAAAC ACCTGTAGTA CATCCTTGGC TAAGGTTAGC CCCAACAGAG

AGGGCTCTCC TCTTACAGAG AACCATTACA TTTGTGCCTT CATCCTAGAG TAGAAAAGGC

ATGATCAGAC TACTAAAAAG ACATCAGGAA AGGGCCTGTG ACATCTGAGG GAAGTGGTTG

CCCTCTCTGG GATGTTGGTT CGGGAAGAGG GGCATGGAGG AGTGCCTGCT TTAGATGGTC

ATTCAGGAAC CCAGGCTGAT AGTGAGAGGT GAAGCCAGCT GGGCTTCTGG GCTAGGGGGG

ACTTGGAGAA CTTTTGTGTC TAGCTAAAGG ATTGTAAATG CACCAATCAG CACTCTGTAA

AATGGACCAA TCAGCACTCT GTAAAATGGA CCAATCAGCA GGATGTGGGC AGGGCCAAAT

FIGURE 16 (83)

AAGGGAATAA AAGCTGGCCA CCAGAGCCAG CAGTGGCAAA CTGCTCAGGT CCCCTTCCAC

GCTGTGGAAG CTTTGTTCTT TTGCTCTTCA CAATAAATCT TGCTGCTGCT CACTCTTTGG

GTCTGCACTA TCTTTATGAG CTGTAACACT CACCGTGAGG GTCTGTGGCT TCATTCCTGA

AGTCAGTGAG ACCACAAACC CACTGGGAGG AACAAACAAC TCTGGACACG CCAACTTTAA

GAGCTGTAAC ATTCACTGCG AAGGTCTGCG GCTTCACCTC TGAAGTCAGC GAGACTATGA

ACCCACTGGA AGGAAGAAAC TCCAGACACA TCTGAACATC TGAAGGAAGA AACTCCAGAC

ACACCATCTT TAAGAGCTGT AACACTCACT GCAAGGGTCT GCGGCTTCAT TCTTGAAGTC

AGCAAGACCA AGAACCCACT GGAAGGAAAC AATTCCGGAC ACATTTTGGT GACCCAGATG

GGACTATCAC CAAGTGGTGA GTACCATCAA CCCCTTTCAC TTGTTATTCT GTCCTATTTT

TCCTTAGAAT TCGGGGGCTA AATATTGGGC ACCTGTCAGC CAGTTAAAAG CGACTAGCAT

GGCTGCCAGA CTTAAGAGAC TAAAGACACG GGTGTCAGAC TTTCTGGGAA AGGGCTCTCT

FIGURE 16 (84)

AATAACCCCC AACTCTTTGG AGTTGGGAGC GTTGGTTTGC CTGGAACCAG CTTCCACATT

TCCTGTACTT CTGGGCTGAG ACGAGGGTCA ACAGAGAGGA AAGCCATTCA GCTCTGGGGT

CCCGACAGCA AGTTGGTTGA CCCTGTGGCC ATGAACAGAA CTCTCGAAGT CATGTTGCCC

AAGCGAGACT CACCCATCTA TCCTATCTAT CCTGACTCTT GCTTCCTGGG TCCTAATGCC

TGGAAGACAA AACTTCCTCT TGTCTCTGTT CTCCAAGGCT AGTCCCACTT CTAAAAACCA

CTCCCTGTCT CTGGTGCTTT TCTAGTTTCT CCTATAAGAA TGATTTCTAG TATAAACTCC

AGGACTCTAT TCTCTTCTTT AGGCACCCGG GCTCACCAAT CAGAAAGCCA TAATTTTTGC

CCAAAGCCCC ATCTTAGGGG GGACTATCTG GAATTTTAGG ATCCCTCCTC AGACAAGCAG

GCCTAACAAA AGCTATTCCT GAAGCTAGGA TATGGGGAGC CTCAGAAATG ATATCCTTCC

TATTCAAGTG AGGACAAAAG GCATCACTCT TCCAATTCTG GAAATCCCTT CCCTCCCTCA

GGGTATGGCC CTCCACTTCA CTTTTGGGGC ATAACGTCTT TATAGGACAC GGGTAAAGTC

FIGURE 16 (85)

CCAATGCTAA CAGGAGAATG TTTAGGACTC TAACAGGTTT TCAAGAATGT GTCGGTAAGG

GCCACTAAAT CCGATTTTTC TCAGTCCTCT TTGTGGTCTA GGAGGACAGG TAAGGGTGCA

GGTTTTCAAA AATGTGTTGG TAAGGGCCAC TAAATCTGAC ATTCCTTGGT CCTCCTTGTG

GTCTAGGAGG AAAACTAGTG TTTCTGCTGC TGCATCAGTG AGCGCAACTA TTCCAATCAA

CAGGGTCCAG GGACCATTGT GGGTTCTTGG GCAAGAGGTG TTTCTGCTGC TGCATTGGTG

GGCTCAACTA TTCCAATCAG CAGGGTCCAG TGACCTTTGC GGGTTCTTGG GTCGGGGGGT

GGGGGGAACA AACAGACCAA AACTGGGGGC AGTTTTGTCT TTCAGATGGG AAACACTCAG

GCACCAACAG GCTCACCCTT GAAATGTATC CTAAGCCATT GGGACTAATT TGACCCGCAA

ACCCTGAAAA AGAGTGGCTC ATTTTATTCT GCACTATGGC CTGGTCCCAA TATTCTCTCT

CTGATGGGGA AAAATGGCCA CCTGAAGGAA GTATAAATTA CAATACTATC CTGCAGCTTG

ACCTTTTCTG TAAGAAGGAA AGCAAATGGA GTGAAATACC TTATGTCCAA ACTTTCTTTT

FIGURE 16 (86)

CATTAAAGGA AAATCCACAA CTATGCAAAA CTTACAATTC ACATCCCACA AGAGGACCTC

TCAGCTTACC CCCATATCAT AGCTTCCCTA TAGCTCCCCT TCCTATTAAT GATAAGCCTC

CTTAATCTCC CCCACCCAGA AGGAAACAAG CAAAGAAATC TCCAAAGGAC CACAAAAACC

CCTGGGCTAT CGGTTATGTC CCCTTCAAGC TGTAGCGGGG GAGGGGAATT TGGCCCAACC

CAGGTACATG TCCCCTTCTC CCTCTCTGAT TTAAAGCAGA TCAAGGCAGA CCAGGGGAAG

CTTTCAGATG ATCCTGATAG GTATACAGAT GTCCTACAGG GTCTAGGGCA AACCTTCAAT

CTCACTTGGA GAGATGTCAT GCTATTGTTA GATCAAACCC TGGCCTTTAA TTTAAAGAAT

GTGGCTTTAG CCACAGCCCG AGAGTTTGGA GATACCTGGT ATCTTAGTCA AGTAAATGAT

AGAATGACAG CTGGGGAAAG GGACAAAGTC TCTCCCGGTC AGCAAGCCAT CCCTAGTGTG

GATCCCCACT GGGACCTAGA CTCAGATCAT TGGGACTGGA GTCGCAAACA TCTGTTGACC

TGTGTTCTAG AAAGACTAAG GAGAATTAGG AAAGAGCCTA TGAATTATTC AATGATGTCC

FIGURE 16 (87)

ACCATAACTC AGGAAAAGGA AGAAAGTCTT GCCTTCCCTT GAGTGGCTAC AGGGAGGCCT

TAAGGAAAAT ATAACTCCCC TGTCACCCAA CTCACTTCAA GGGTTAATTG ATTCTAAAAG

ATATGTTTAT TACTCAATCA GCTGCAGATA TCAGGAGAAA GCTCCAAAAG CAAGCCCTTG

GCCCTGAACA AAATCTGGAG GCATTATTAA ACCTGGCAAC CTTGGTGTTC TATAATAGGG

GCCAAGAGGA GCAGGCCAAA ATGGAAAAGC GAGATAAGAG AAAGGCCACA GCCTTAGTCA

TGGCCCTCAG ACAAACAAAC CTTGGTGGTT CAGAGAGGAC AGAAAATGGA GCAGGCCAAT

CACCCAGTAG GGCTTGTTGT CAGTGTGGTT TGCAAGGACA GTTTAAAAAA GATTGTCCTA

TGAGAAACAA GCTGCCCCCT CACCCATGTC CACTATGCTG AAGCAATCAC TGGAAGCCAC

ACTGCCCCAA AGGACAAAGA TTATCTGGGC CAGAAGCCCC CAAGCAGATG ATCCAACCAC

AGGACTGAGG GTGCTCAGGG TTAGCGCCAG CTCATGTCAT CACCCTCACT GAGCCCTGGG

TACATTTAAC CATTGAGGGC CAGGAAATTG ACTTCCTACT GGACACTGGT GCGGCTTTCT

FIGURE 16 (88)

CAGTGTTAAC CTCCTGTCCT GGACAGCTGT CCTCAAGGTC TGTTACCATC CGAGGAATCC

TGGGACAGCC TATATCCAGG TATTTCTCCC ACCTCCTCAG TTGTAACTGG GAGACTTTGC

TACAGATAGT AAGTATGCTT ACCTAATCCT ACATGCCCAT GCTGCGATAT GGAAAGAAAG

GGAATTCCTA ACTTCTGGGT GAACCCCCAT TAAATATCAC AAGGAAACTA TGGAGTTATT

GCACACAGTG CAAAAACCCA AGGAGGTGGC GGTCTTACAT TGCCGAAGCC ATCAAAAGGG

GAAGGAGAGG GGAGAACTGC AGCATAAGTG GCTGGCAGAG GCAGGGAAAG ACAAGCAGAA

AGGAAAGAGA GAAAGAGCAG AAAGTGAGAG AGAAAGAGAG ATAGGAAGTG ATAGCAAAGA

GGGAGTCCGA AAGAAAAGAG AGAGGAGAGA GAGAGGGGGA AAGACAGAGA GAGACAGAGG

AAGAGACAGA GAGACAGAAA GAGAGAAGCA AAGAGAGGAA GAGACAAAGA AGGAGTCAAA

GAGAGGGAAA GAGAAGTAGT AAAGAAAAAA CAGTGTACCC TATTCCTTTA AAAGCCAGGT

TAAATTTAAA ACCTATAATT GATAATTGAA GGCCTTTTCT GTAACCCTAT AATACTCCAA

251/285	262/285
252/285	263/285
253/285	264/285
254/285	265/285
255/285	266/285
256/285	267/285
257/285	268/285
258/285	269/285
259/285	270/285
260/285	271/285
261/285	272/285

FIGURE 16 (89)

TACCACCTTG TTGTCAGTGT AAACAAGGGT ATAGCCCAAA AGCACTGAGG CCACTGACAA

CCCGTAGCCT TCTTATCAAA AATCCTTAAC ACAGCAGGTT TCCTAACAGG GAATCTAAAT

CTTAAGGTCG GACCAGACAT AGGAGGAACT GCCTTCAGGA CAGGATGATA GATGGTTCCT

CCCAGGTGAT TAAGGAAAAA GACACAATGG GTATTCAGTA AGTGATAAGG AAACTCTTAT

AGAAGCAGAG TTAGGAAAAT TGCCTAATAA GTGGTCTGCT CAAACGTTGA AGCTGTTTGC

TGTTTGCACT CAGCTAAACC TTAAAGTACT TACAGAATCA GGAAGGAGCC ATCTATACCA

ATTCTAAGTT AATATGGACT GAACGAGGTT TTATTAATAG CAAAGAAAAT TAAAATCTCA

AACTTACAAG GTTTTCAACT AAAGTAAAGT TTGCTAAAAG TTAACAGCGT AACATGTATT

ATCCTACTAC CTCACACTCT CTCAAAGGAT TTCTCAGACA GTTTGCAAAA AAGAACGAAA

TCTGTCCTTA CTCTACAATC CCAAATAGAC TCTTTGGCAG CAGTGACTCT CCAAAACCGC

TGAGGCCTAG ACTCTCTTAC TGCTGAGAAA GGAAGATTCT GCACTTCTTA GGGGTAGAGT

FIGURE 16 (90)

GTTGTTTTTA TACTAACCAG TCAGGGATAA TATGAGATAC CACCCAGTGT TTACAGGAAA

AGGCTTCTGA AATCAGACAA TGCCTTTCAA ACTCTTATAC CAACCTCTGG AGTTGGGCGA

CATGGCTTCT CCCCTTTCTA GGTCCTGTGA CAGCCATCTT GCTAATAGTC GCATTTGGGC

CCTGTATTTT TAACCTCTTG GTCAAATTTG TTTCCTCTAG GATCGAGGCC ATCAAGCTAC

AGATGATCTT ACAAATGTAA CCCCAAATGA GCTCAACTAA CAACTTCTGC TGAGGACCCC

TGGACCGACC CGCTGGCCCT TTCAATGGCC TAAAGAGCTC CCCTCTGGAG GACACTACCA

CTGCAGGGCC CCTTCTTCAC CCCTATCCAG CAGGAAGTAG CTACAGCGGT CATCGCCAAA

TCCCAACAGC AGCTGGGGTG TCCTGTTTGG AGGGGGGATT GAGAGGTGAA GCCAGCTGGG

CTTCTGGGTC AGGTGGGGAC TTGGAGAACT TTTGTGTCTA GCTAAAGGAT TGTAAATGCA

CCAATCAGCA CTCTGTGTCT AGCTAAAGGA TTGTAAATGC ACCAATCAGC ACTCTGTAAA

ATGGACCAAT CAGCAGGATG TGGGCGGGGT CAAATAAGGG AGTAAAAACT GGCCACCCGA

FIGURE 16 (91)

GCCAGCAGTG GCAACCCACT CGGGTCCCCT TCCACACTGT GGAAGCTTTG TTCTTTTGCT

CTTCACAATA AATCTTGCTG CTGCTCATTC TTTGTGTCCA CACTACCTTT ATGAGCTGTA

ACACTCACTG CGAGGGTCTG TGGCTTCATT CCTGAAGTCA ACAGACCACG AACCCACTGG

AAGGAACAAA GAACTCCCGA TGTGCTGCCT TTAAGAGCTG TAACACTCAC TGCGAAGCTC

TGCAGCTTCA CTCCTGAAGT CAGTGAGACC ACAAACCCAC CAGAAGGAAG AAACTCTGGA

CACACCTGAA TATCTGAAGG AACAAACTCC AGACACACCA TCTTTCAGAG CTGTAACACT

CACCGCAAGG GTCTGTGGCT TCATTCTTGA AGTCAGCAAG ACCAAGAACC CACCGGAAGG

AACAAATTCC AGACACAGTA GGAAATCTGT ATTTTTGATC TGTGGCTTCC AGGGTTACTC

CAGTCATTGA AGTCTCCATT GCAGCCTTAA GGAAACAGAG AATGGTTTGG AGGAGCACAT

GTGGGAATTG TTATGGACCA GGCTTGAGAT GCACATAGGG CATTTCTGAT CAAACCTAGC

TGGAAGCAGG GCCAGGAAAT ATAATCTAAG GAAGACAGTT TTTGTAGACA GTAGTAGTCT

FIGURE 16 (92)

TTGCATCTGA GACATGTAGA TTATCAAGCA ATTAATTAGA AAAAATATAG CCAGGTGCGA

TGGCTCATGC CTGTAATCCC AGCACTTTGG GAGGCCAAGG GGTGTGGATC ACAAGGTCAG

GCGTTCGAGA CCAGCCTGGC CAACATGGTG AAACCCCGTC TCTACTAAAA ATACAAAAAT

TAGCCTGGTG TGGTGGCACG CATCTGTAAT CCCAGTACTC AGGAGGCTGA GGCAGGGGAA

TCTCTTGAAC TTGGGAGGCA GAGGTTGCAG TGAGCCAAGA TCACACCACA GCACTCCATC

CTGGGTGACA GAGCGAGACT CTGTCTCAAA AAAAAAAAAA AAAAAAGGAA AGGAAAATAT

AATCAAGAAT ATTGACAGGT AACATTTATT CAACACTTAC TATGCACCAG GCAATACACT

AAGTGTTTTA CATGGATTAA CTCATTTAAT CTTAACAATA GCCCTATGAA GTCAGTGCTG

TTATTATCTC CACTTTATAG ATAAGGAAAC TGAAGTACAG AAAGGTCAAG TAGAGAAATG

GCCATGCTTG CATTCTCAGT TTTTGAAGCA ACTGTTACAG GAATCTGGTG TGAGAAATGC

TCTAACAAGA TGTGAGTCAG GGGTTGGGAG GTACTGAGTC TGAGTTGGGC AGTTGGGGAT

FIGURE 16 (93)

GGAAGGATGG ATGAAGAACA GCTTGACAGA GAAGCTGACA CTTGGCAACT CTGTGGGACC

TTGAAGGGTT AGAGGGACTT CACCAAAGAA ACTGGTGGTC AGGGAAACGG GAGGGTCACG

GCAAGGAGGG AAAGGAAACT GTACCACAGC AGAGAGTCTG AAGCTACTAC AGTGTAGTTC

AGCGTATAAA GAATAATTAT TTTAAGGTAA ACTTATAACC TCATGCAAAT ATAAAATGAA

CACGTGTCAA AGATCTTATT TAATTTATTA ATTAATGAGG GAACCTGTAA GATGTTACAG

CCAGTTCAAA GGATAATTCA AATAAATCCA TGCACATATG TAGGCAATAA GGAATGCTGA

AATGAATTTA AAAGTAGATG TAAACTGATT TATCCACAGA GAAATAATCA GTTGCATTTC

ACATAACAAA ATTCAGTTGC TTTTCTACAG AAGGAATTGT TTGCATCATT ACCAATTTTT

CTACAACTAA CAGAATTATA AAATAACTCA AACACAATGA AAGGCAGATA TAACCCACAA

TGGTATGATA GATACAATAT CCACATCCAG GATGTTTTTT TCTCATTTCA AAGTCTTTCA

CAAGTTTTCC TGATAAGGGA GTGTCAATAA TACTGTATGG CAGGCAATAA GACTGGATGG

FIGURE 16 (94)

ATGGTTGGGG CCAGGTTTTA AGGGGTAATA AATGCCATGT AAAGGTATGT GCATACTGTG

CAACATGTCG GGGGAATCTC AAATTATTGG TAGAGTATGT AGGAAACACT TGTGGGAGCT

TGTTAATAAA TTCAAATTCC CAGACCCAAC TCCTCAAGGG GTCTAATACA GTAGGTTTGG

AGTAAAGCCT GAAAATCTGC AATTGTGCAA AAAAAAAACC CAGGTGATTC TGATACACTT

TGAGAAGCAC TGGTGGAACT AATAGTCACT GAACGTTTTT GAGCAGGGGA GAAACCTGAG

GACGTCTATG TTGCAGCAGT GGAAACTTGA TTAGAAGTAG GAGAAGATGC ATGGTCTTAA

AAGAATGCAA AATGATGGCT AATATTTGAG TGCTTATGAT GGGCCAGGGG CTGTGCTAGG

CGCGTGGCAC ACATTCAATA CGATGGAAGC CTGTACCAGT CAGTATTAGT GGGGTATCTT

TAAGAGTGAC CAGAATTAAG GGGGGTTTTC ACCAAAGCCT GAGGACTGAG CCTCCTCATC

CTAAATTCAG ACACAATGCT GTACCTATGC ATTTGCCTCC AGGCTGTTCC TGGGCCTCCA

GGGACTGGCC CAGGCTCCTG ATAAATAGGG ACTCCCAACA ACATAAAGCC TGGATTTTGG

FIGURE 16 (95)

AACTTCCTGA ATGTTACTCA GGCTTTCTAG TAACTGTGGA GATCTGAATA ATAACACAAT

TCTAAGTTCC CCTACTCATA AAGCTGCTCA TCATTTAGAT GGGGTAAAGC ACCTGAAATA

CAATGAGCAT CACTATTTTC ATTCATCCAT GAAATGAACA TTCCGGGGAG ATCAGTAAGT

TGATGTATCA CCCTTGAACA GGGCAAAATG AATACTCACC AGGAATATGT GGTATTTTAA

AAAGAAGGCA AAGGGAAGAA TAGTGGGGAT GGGGCAAAAA CTTTAAATAG ATTCCCCCAA

TCATATATGG CAATTGAAGA TAATTAAATT ATCATTTTAA TTGAGTAAGT ACTCATAGAG

CCCTCACTAT TTGAAAATGA ACTGCCTCCT AATTGTTATT GTGCAAATGT GATACATTAA

ACTTAAGCTA TTTTAATAAA ACATCCATTT TCGGAAGCTG TAGTAGGTTC TCCCAGGTCA

GATTTGATAA GCCATAAAGA ACAAATGCCA ACTCCTATTT TTCTATGGTG CTGGGAAATA

AGAGAGAAAT GTGTAATTCA AAGCAATCAT TTAATTTTAT CCAATAGCTT GATTCTCCTC

TCTCTTCTAG CCTTTTAGCT AAGCTGTTAC CAAGTAACCA CACTAGTTGG CTTGAGTCTT

FIGURE 16 (96)

ACCACTGTTT CCCTGACCCC ACAGTGGAGA GACTGCATCT GTTAAAGAGC AGTTATGTAA

CCATGGCTAT GCTGAGCTGG GATTCCCAAG GCTTAGGTTC TTTCTGTGAA TGACCTTCAC

CAAGACACCT GAGGTCTGTG TGGAACCACA GGCTTGTCAT CTCTAAGGCA GAGTTGATAA

TTCCATCTGT TTCTTGAGCC CACACTGAGA AAAAGATTAC ATGACTGCAG TTATTTGAAT

GCCTCATGGA AAGACGTCTT ATAAATATTA TAATTAATGT TATCATTAAG TAATGCTTCA

ATGCAGATCT TCCAAGTATA AATATCAGCT GAGTAAGAAG TCAATCTTCC CTGAAGCAAA

ATTGAAATTT GTAAATGCGA TTTCTGGGAG CTTATTTTGT AATACATGAT TCCAGAGTGT

CCATAACACA CACAATTGTC TTTTTTCCCC TACATGGGCT ATTTACAACA AAATTGGACT

TATAATGTTT ATTTCCAGGG ATGACTAGAA CTTTAATAAC AAACCTTGGG CCAGGCATAG

TGGCTCATGC CTATAATCAC AGCACTTCGG GAGGCTGAGG CTGGTAGATT ACTTGAGGCC

AGGAGTTTGA GAACAGCCTG GCCAACATGG CAAAACCCTG TCTCTACTAA AAATATAAAA

FIGURE 16 (97)

ATTAGCCGGG TGTGGTGGCG CATGCCAGTA ATCCCAGTTA CTAAGTAGGC TGAGGTACGA

CAATCGCTGG AACCTGGGAG GCGGAGGTTG CAGTGAGCTG AGATTGCACT ACTGCACTCC

AGCCTGGGTG ACAGAGAAAG ACTCTGTCTC AAAAAAAAAA AAAAAAAATA ATAATAATAA

TAAACCCTGA TGAAAGGTTT CTAAAATGTT TTCATCTAAT GGTTTTCTTG ACAATTAAAT

TTTCTATATA ATGTCAGTTC ATAAAAAAAC TGAGAACGAC CACATGTCAT ATCGACTGCT

TAAAAGAAAA TACGTATATT TACAAACATA TACACGATAC TGTCTTTTGT CTGGTTAGTT

TAGAGGTTAG ATAAACTGCA GTATGTTGTA GTGGACAGAT CATAGAACTA GGAGTCAGGA

TGTCTGGATT CCTAGGAAGC AATGAATAGG TTGCACGGTG CAGACCAGCA TCATGAGTAT

CCTCAGGGAG CTTGTTAGAA CTGCAGATCC TTTAACTCAT TGAATCAGAA TCCCTAGGTG

TGGGGCCCTG AAATCTGTAT TTTAGCAGGC TCTCTGGGAT TGTGATGTGC CTTAGAGTTT

GACAACCACT GGGTAGCTGA TCCTGACTTA GACTTATCAG GCATGTGATC TTGAACAAGT

FIGURE 16 (98)

CACATAATCT CACTGAGTTC AGTTTTCTTA TGCTTAAAAT AGGCCCAATA ATATCTATTT

CACATGGACT GCTTTGAGGA TTAGGCAAGA GATCTGTAAC AGACACTGTA GAACAGTGTC

TCTGGTCTAC AGCTGACCTT CCATAAATGG TAGTTGCCTT GATCTCTGCT CTGCCACATA

ATAGCTGGTT AACTATGAGC AAGTAATTTA GTTCTTCTCA GTTTAGTTTC TTCACCTGTA

AAAGAAGGAA AATAACTGTT ATACTCAATT TCTGAAGTGG CTATAAAAAT CAGTTTAAAT

TATGGGCATT GAAGCTCTTT GTACACTGTA TAAGGACTGT ACATCTAAGG GATTAATGAG

ACCAGGCTTA TGATTTTAAG CATGGAGTAA ATAGTAACAC TGACTCTGTT CTATGAACCA

CATGGAAACT CTAAAGAATA TGCACATTTG AAACACAGGT ATCATCTGGG GAAGGTGATC

TGCTCACCCA AACCAGTTCA TGAACATCAA TCTCCAGTGG CGTGCTGGAG CTAGCTGTAC

CAGCTCATGA GGGCCAATTG TTTCATTTTT AGGAATTTTG TTTGCTGGTT AAAAATAGTC

ATTATTTAAA ATTAAATTAT GTAAACAATA ATATTAGATA AAATAAGTTA AAATAAAAAC

FIGURE 16 (99)

AAAGGAACTA ATTATCCCCA AACTCTTCCC CACCTAATTA TTTTACTATC TGTGCCTTGG

GATTATTTAC ATTGATTTTA TCCATATGGT GACAATACTA TTCATATATA AATGGTGTGC

TTCTCTTCAT AACTCTACAT AGCCTGATGT CAGGCTAGTA GCTTGAAATT GGCCACAGTG

GGAGTGTGAG CATTTGTACC ATGAGGCTTG GCCAAGGCTA CAAATCCAGA CTTTTGTTTT

TCCCTCCTGG AGAGCTGTCT GTTAAAAATT TACCAACACA CCACTGGTCT TACCTTTGTT

AATTTACCAC AGTCCAGGTT CTGACCTAGA CTTAGAAACC TGGATTTGTC AGCAAGCTGA

GGATAGAGCC ATTATTTTTA AGAAGGACTC ACATTACCCA AGTGCAAAGC CTGATATATA

CCTTCAGAAT ATCAATTTAT TAATTTACAG TGAAGAAAGC CACCCCAGGG CATTCCCCAG

GGGAAGGCAA AAAGAGCTAG TTGCACATTT TGAATGTTTG ATGACATTAG GGTAAGGTGA

CACAGAATAT CCATTTCCAC AACTGAGATA CCTGCTGCCT TAAGGAAGGG ACAGGCAAGT

CCTTGGGCAG GACCTTAGAT TGTCACTGTC CATCTTGCTC TAGGACTCTC CTTTCCAGGC

FIGURE 16 (100)

ATGACGATGG CCAACTCTGT CCTCCTACCC TACTGATGGG ATTATCTTTT CTTGACACAT

GGCAATGCCT CCAATCAGAG GCTGGTAGCT ATTTTTAATC TTCAGGGCAG TATTTTTCAA

AGGGAAGTTC ATGGACCATA TGCATCTGTA TCATTTAGAT GTATATTAAA AATGCTTAGT

CTTCCCCAGT TATACTAGAT CAGAATCTCT GTTGGTGGGG CCCACGAATC GGTATTTTCA

ACAAATCACT AGGTAATTTC TGTATATACT ATAGTGTGAA GACCACTGCT TGAAGGTTTC

TTTGCATATC TCCACTAAAT ATAAAAAATA TTGACTTCTA GATTTAACTC CCAAAGCACT

TGCATTTTTA AGTTTCTGGG GGCATTATAT TGTGGTACCC CTATACCACT CACACTCTAG

TCAGGAGGTA TATTATGGAC TGAATGTTTG TGTCCCTCCA AAACTCATAT GTTGAAGTCT

TAGCTTCCAA TGTGATAGTA TTAGGAGATG GTGCCTTCTG GAGGTAAAAT CAAGCCCTCA

TGAATGGGAT TAGTGCCTTT AGAAAGAGAG CTCCGTCACT GTCTTTCCAT CAATTGAAGA

TGCAGTGAGA AGCTGGTAGT CTTGCATCTG GAAGAGGGCC CTCACACAAC CTGATCATGC

FIGURE 16 (101)

TGGCACCTGG TCTCAGACTT TCTGCCTCCA GAACTATGAG ATGATAAATT TCTGTTGTTC

ATACCCCACC CAGGCTACAA TATTAGGTTG CTGCAAAGTA TTTGTGATTT TTGCCTTTAC

TTTTCAGGGC AAAAACTGCA ATTACTTTTG TGCCAACCTA ATATTTTGTT ATAGCAGCCC

GAACTAAGGC AAGGGAGACT ACATCAGACA GTGTAGCTAT GTAAGTACAA ATGTATCCCT

GTTGAGGAAA ACTAAGTTCT AACCCTGACT TCAGGCCAGT AGCCACCTTT TCAATCTCTT

TCATGAAGGG ACCATTATCA TTATCACTGG TGGCAAAAAT AGAGGCACGA GAATGGAATT

TGCTTTTCTG TGAAATCTCA GTGTATACAG ATTGAAGAGC AAGGGTTTGC TTTCATCTCT

AAGAAGCAAA AGTGAGTACG GACTGGCACA TTATCAGAGA AAGAATCATT CTAGCTCGGT

GGGTCTTAAC CAGGAGTGAA TTTGACTCCA GGGAACAGTT GGCAATGTCT GGAGACGTTT

TTATTTGTTA TAGCTGGGGG ATGAGTGGGT GGGTTGCTAC TGGCATCTAG TGGGTGGAGA

CCAGAGATGC TGTTAAACAT CCCGCAAAGC ACAGGACAGT CCCCGACAAC AAAGAATTAT

FIGURE 16 (102)

CTGGCCCCAA ATATCAATAG TGCCAAAGTT GAGAAACCTC ATTCTAGCTT CCTTTTCCCT

TCTACGTTCT AATCAACTGT TGTTCTTTCA GCATTAGGAT TCATCCAGCA GTCTCTTTCC

CCAGCAATTT GTTGAAATTT TTTTAAAAAT GGACTCATTT TAGTGTCACA AGAAAAAAAT

ACATTCACAG GAAAGGATGG GTCATTTTGT TTAATGATGT TTTGCCTTTC ACATAGCAAA

AGCTTAATAA AGTATTTTTA AATAAAATGG TGAATAGATC AAAACATTAA TTTCACATGT

GTTTTAATAA ATAACAGGAA GATGGCTATA TTATATAAAT TGTTCTTGTA TATGTCTTGA

GTGGATCATC AAACACAAAC GTATCTACAT GCCTTTTCTT GTGAATAGAT CTAATAATAA

CGCTCTTCTA AAAACAAATT AAATGGATAT TATTTGCTGA GAATGTAATG CTTGTGTGAA

TAGAAGCCAG CCCTGAATCC AAGCCCCCAG ATCTATTTAA AGAATTTGAA GAATGTCAGA

AAAGCACGTG GCTTCAAGGT TAATGTGTAA GACTCACAGA AACTTGAAAA ATCACTATGA

CTAAAAAGAA AGTATGAGCT CCCTGCATGC CTGTAAATTG GAATGACAGC CAAAACCAGT

FIGURE 16 (103)

TAATTATAAA AACAGCTAAT TTAACAGGTT TTCAAATTTG TTTCTTTCTC CAAGTAGCAT

ATAGTCAATA ATCCTTAAAG AGAAAGCAAA GAAGGGGAAG CACTGAACCA AATTTGCTTT

TTTGTACCTG CTCAGCTCAA ATGCAGAGTT CTCTACCTGG AAATTGACTG CTTCCATAGT

TTGATAGCCA CAGAGAGATG GGAACAGAAG GAGAGGTATA ATCCCAGACT TGATTCAGCT

ATAGAGAATG ACAATAGTGT CAGAGGCCTT CCAACCAGAG CGACTCCATC TTGAATACGG

GCTGGGTAAA ACAGGGCTGA GACCTACTGG GCTGCATTCC CAGGAGGCTA AGCATTCTAA

GTCACAGGAT GAGACAGGAG GTCAGCACAA GACCTTGCTG ATAAAACAGG TTGTAATAAA

GAAGCCAGCC AAAACCCACC AAAACCAAGA TGGCCATGAG AGTTATCTGT GGTTGGTCTC

ACTGCTCATT GTATGCTAAT TATAATGTAT TAGCATGTTA AAAGACACTC CCACCAGTGC

TATGACAGTT TACAGGTACA TTGGCAACTT CCGGAAGTTA CCCTCTATGG TCTAAAAAGG

GGAGGAACCC TCACCTCCCA GAATTGCCCA CCCCTTTCCT GGAAAACTTG TGAATAATTC

FIGURE 16 (104)

ACCCTTGTTC AGCATATAAT CAAGAAGTAA CTGTAAGTAT CCTTAGGCCA GAAGCTCAGG

CCACTGCTCT GAATGTGGAA TAGCCATTCT TTTATCCTTT ACTTTCTTAA TAAACTTGCT

TTCACTTTAC TGTATGGACT CCCTGTGAAT TCTTTCTTGC AAGAGATCCA AGAACTCTCT

CTTGGGGTCT GGATCAGGAC CTCTTTCCAG TAACAATAGT AGTAAGGGGT CAGGGAGACT

GGACAAAGGA GTTTAAGAAG CCTTAGATAA AGGGTCCTCA TCATTGTCAT AACATAAAAT

CATGGACTCC TAGAATTTTA TAGCTGATAG GATTAGAAAT TTCAAAATTC AATTTCATTA

ATTTTCATCT GCGAAAACAG ATGGCCAGAG AGGCCAAACA ATTTGTTAAG GAGCACTGAG

GGCAGACCAC ACTGGAACGC AAACCTCTTA GCAGAGTATA CAAGGCCTTT GATCTCCTCA

GTCAGAATGA ACTAGAGCTT TCCAGGGTAC CCTTTCTGAC TGTTTAGCAT GTTTGCCAGT

CTGACTAATT TTGAAGTTGC TTAAATATCT GTCATTTCCA CTGTATCATA ATCTCCTCAT

TCATCTTCAA TCTCCAATGC CTTGAACTCA GTAAATGTTA GTTGAACAAA AGTAAATTGA

FIGURE 16 (105)

ACCCAGAATT TCTGATCATA ATCTGGAGCA CTTTAAAATT GTCAGCTTAC TGGGAAACGG

GATAACATGT GATTTGTCTT TGATTTTTTT TTTCTCATAT GCTTTTTCCA CCTATAGATG

CTACACGAAT GTTTTTAAAA TCTGATATAA AAATTAAAAT TAAAAAATTA AAAAAAGAAA

ATTTGATACA ATGCTACATT TAGAGTGTTG TGATTAGATT CCTTAAGTGT ATCATGGTGA

TCTCTACATC ACGTGGTGAT CAAATTGCTT TGGGTTTTAA CACATAACTG ACAAAGGCTT

GGGGACATGT AAGATCCCAA ATACATTTTT ATTGATTTTT TTTTCTTGTT TGTCCTCTTT

TAAATAACTT TTTTTTGTTA TAAGAATAAT TCATGTTCAG TGGAGAAACC ATAGAAAATA

GTGACAAGTG AAGGAATAAA TTTAAAATGA CCCATAATTG TACCATACAT TCTGATTTTT

TAAACGCTGA ACAAATTAGC CTTGGGTAAG TACCAGGAAT AGAGTGCAGC ATTGAAAGTT

AAAGTTTGGG GAAGGATAGC TGACTTAAGA AATTATCTAG TTAGACATTT TTTGATGGGG

TAATTTTGCA GATGACATTA GTGAGAGAAA GGACTTGCCA CTCTCACACA GCTAGTAGGG

FIGURE 16 (106)

GTGTGGGAGG ATATTGGAAC CAAGTTTCAA GTCTTCAGTG AAGAATCAAG GGAGAAGTTC

TAAAACCTAA CAATATCCCT CTGGATGGAC ATTTATTTTA TTACTACAAT AAGCCACACG

GTGAGTCATA AGGAGCATTT CATTCTTCTA ATATGTCTCT ACTGTATTTA GAATCTGATA

AAGCCCCTAT TAGAATTCAT CTCTTTAAGA ATAAAAGAAG CTGAGGAACT AAAGAGAGGG

TTGGAATAAT CCACTAATTA TATCCGTTAA GCTTCAGTTA CGCTAATAAG GAATATCACA

TGACTGTGGT GTGTGCTTGT TCTGAACAGT AAAGTACATG AGGAAAGATA AGATTCAGGG

CTGAAATGTC CTTCAGCATA TGTAGGTAGT GGTGATGAAA GTCATTAAAA GAAAAATTGA

TTGAGGTATT TTAGTAAACA AAAGAACTCA CCACTTACCC ATCAGGAAGT GTATTGTTAA

TGCAGTGCTG TTCAGCCTTC TGGAAGAAAA GGTTTCTTCA TGCTTCTCTC TTTAGCCTAA

TTCTTATCCT GTCACTTTTC AGGCAAAATT AAAAAAAAAA AAAGATTGAA AACGATGCTC

CTATTTTATT TGCTTCAAAA GAAACAGGCT GTTGCATTGT GCTTGGAACA GTTTACTCTT

FIGURE 16 (107)

GGCCTTGATG TAAGTGTGAA AGGAAGCCCA TGTAATTGAC TAGGCAGTAT CTGAAGAAGC

AGGAAATACA GTGTTAAGAA AATGAACAGG CATGAAAACC ATGGCTATTT GATAAAAGTA

AATAATTTCT GCAGTTCACA TGTTCTCAGC ATATTTTCTT TGATACTGAC TTGCTTAATA

TGACAATAGC AGAACCATGG TAGCTTGTAG GCATTACTTT TCTTTTAATT TCTTTTACAT

TTTGAATTTA CCAGCACTCA CATTTGTATT ACTTTTGGGT TATACTGAGG ATCTATAACT

TATAGATCAA ATACCTGACA TATATATGCA TTCTCTGAAG TCTTAGGGCA GAACTAGAAC

ATTCTTGTGA ACATCAGTAT AAGATATTAA AATGGAAGTT TTGCCTAAGA CTGAAGACAA

TAAAAATATC ATAGTCTGAA ATGAATGCCA GCACACCATA CAGGATTTAA ATATCTATAC

ATATATATGT GTGTGTATTA TATATATTTA ATATATATCT GTGTGGGATA GGAAGAGGTA

GGGGGAAATC AGTTTTACAA TTATTAAGTA TTTCACCCTT GACAAGAGTA TATATATTGG

AAATCAGTTG GAGAGTATTT TCAAAGATAA ATGTTAGTGT GCTATGAATG AATCCACCCC

FIGURE 16 (108)

TACCACCACT GAGGCAGGGT AGGAGAGGCC TGTGCTCCTC AAGCATAGTT GGAAAAGGAC

CTCAACAAGA CCACTTCAAG AGTCTAATGT GTGGAGACTG TTGCTTAGGG AGACCTTATG

GTCTAGCTTC TGACTCACAG CTAAGTCAGG GAGACAGGTT GGCTGCTCTG ATCGTGGAGT

CCAAAAGATG GCCTGCACTG AAAAGCCTCA TGAGTGTTGA CTTAGGGCTA GTCTAAGAGG

TCCCTGGAAG AAGAAACACT CAGTAGGAGA GAAGCTGGAG GTACCTTCAG TGCTGAATTG

GAACCTAGAT TCATTCCCCC GTGGAGCAAA TTACATAGGA AAGATGCCCA GTGATGGAGA

GTGGGGGTGT CTCTAACAAT TACCCACCCA CCTGCCCCCA CCCCTAAGAA AAAGAAAATC

ACATACAACC AGTCAGCTGT AAACATATGC CGAGCCTAGT AAACTCAGAT ACTAAGTTAC

CAGGGTACCT GGCAAGTAAG AACATTCCTG ATTCCCTTCC CTCCTCTTCC TCTTTGCCCT

CCAACCTTAG TGGCTAGCAA GATGGGGAGA GGAGGAGAAG CTGTAAGTGG GGAAAAAAGA

GCAGCTTTCT CTCCTTTTCA GCTGCTGGAT TCTCCCTCAT CATAGGCCTG AGCTGGGGAA

FIGURE 16 (109)

```
TCAGGAAGAA GGATTCTTTT TAAAACTGAA GTAACGTTAT CATTTAATTT TAAAACATTT
TAAATTTTGA CAATGTTGAG ATTAGATATA CTAATTATTA AACTAAGATT ATGTTTTGCA
GCTTGAAGTG ATAAGAAAAA CCTCTTATCT AAGAGCATCC AGGAAAGTCG GGGGTTTCCT
GAACATCCTT TTAAATCCTT TGGAAGTCAG CTTTCAGAGA GGATTTAAAG TGTAGACTGG
GCCTTCAGAA ACTTGGTTAA TGTAGGGGTT TCCTATGCAG ACTTGGGGAC TATACCTTGT
GTGGAAGAGA GAAAATAAGA TTATCTTACA TTTTTCCCAT TCCTTTTTCA AAAAGAAAGC
TCAGCTAGCA TGAAAGTTAA ATTCAAAACG TAATGGGTAT TATTTGCATA TTCAAATCTA
GTGCATATCA TGTAAGTACT GAATTATGGT ATTCATTATT TCAAATGACA AGCTGGATTT
TTTTTTCTTT CGAATTTCAC AAATTAATTT TCCTTGGAAC CTTTTGGTTT GGGCTTTAAG
AGTTTAGGCT TTCATCACAA AGAGAGGACA GCCTTGAAGA TTAAAGTGTG TGGCTCTTCT
CAAGATGTTC TTAGTCCAGC AAAGGATTCT ATGCATATTT GGGCTTCCTT CTGTCTCATA
```

FIGURE 16 (110)

ACCTGTATTT CTTGATATTC TATTTATATT CTGTAAGATT TTTTTTTTAA AGGAAAAATT

CTTCCATGGT TGAAGGACAT GTCAAAAATA GAGGATACAG TTTTATATCA AAGGAAGTTT

CATGATATGA CTGTAGAAGC TCATTTGACT TAAGACACAT CATTTCCTCA TGGAAGTGTT

AAACAGATCT GTACAATAAG GTTGGCAATC TTTGTGTAAA ACAGTTTTTT TTCTCCTGCT

CTAAAGAAAG TGTATATTTC AAAATGTGAA TGTCAGCAGT CAGAAAATAG TATTTTTTTA

ACTTCGTTTT CAAAGTCCTC AAAAACCTGT ACCTAATCAT GAATTTTTTT TCCCACAGAT

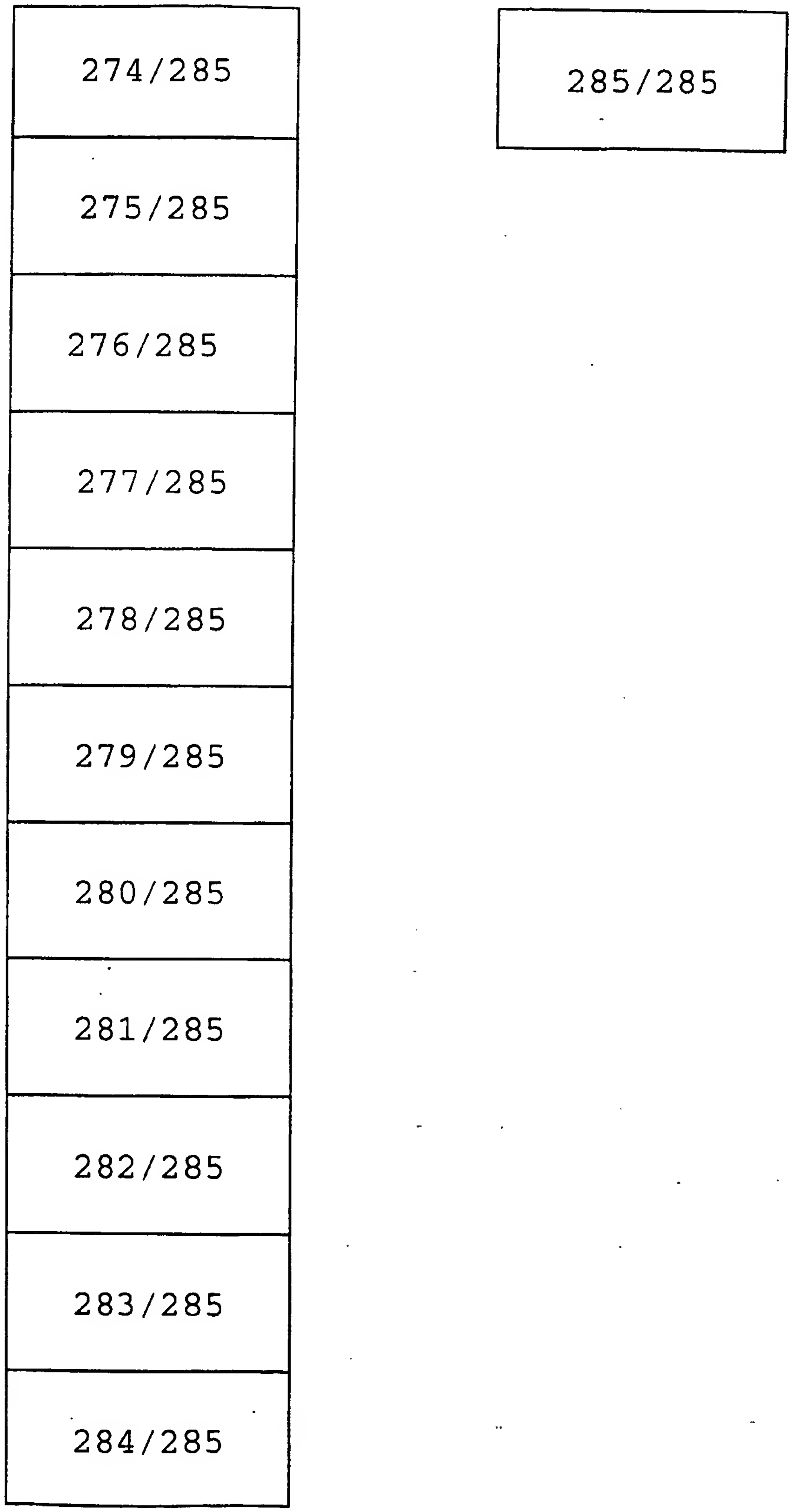
TGTTTCTTCT TCTCCCTCCC AGAAACTTTG AAGTTTTTCT ACATGACACC AGGACCTATG

TCTTTTTTTA ATTACACAGA AATGAAAGAA AAAAAGTGTG TTGTATCGTT AACCAAATAT

ATGAAATCTT TAAGCTGTAT TTTTATTTTT AACTTTGTTT TGCAAAGAGG CCATTCCCTT

TGGTTAAATA ATTTGTTATT CACAGTTTCC TTGTCCTCAT ATTATCAAGG GGAAAATTGT

AGAAATTTTA AAGGAAGCTC TAGGCAATGT TTTCATCCCT GAATCTTTGG AGAGTTATAA


274/285
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284/285

FIGURE 16 (111)

AAACAAACAG ATTACTGAAC CTGTAAGAGA ACCAATCGTG AAGTCATTAC ATCTAAGCAT

AAGCAAAATC TCCTCTTGGA TCATTAAGTT ATAGAAGAAA AGAAAGCCTG CACTTTGAAA

TTTAAATAAA GCTTGGTAAC TTGTAAGTCA AACACGTAAA ATTTTACAAT TCAGGAATAT

CGATAGCAGT TGAGTTTAAT AGACTTCTCA CATTCCAAAT TTAAAGCTTC CTTCTCTGTG

CTAATAGAGA TACAATAGCA GTAGGCGTTT AAGAAGAATG AATCAACAAT TTAAAACTAT

AATGTGTTTT TTATTCATCT CCCTTATTCA CATATATTTG TTTTGTTTTG AGAAGGAGTT

CTGCTCTGTC GCCCAGGCAG GAGTGCTGTG GCACGATCTC AGCTCACCGC AACCTCTGCC

TCCCGGGTTC AAGCGATTCT CTTGCCTCAG CCTCCTGAGT AGCTGCGATT ACAGGCGTGC

GCCAGCAACC CCGGCTAATT TTTGTATTTT TAGTAGAGAC AGGGTTTCAC CACGTTGGCC

AGGTTGGTCT CGAACCCCTG ATCTCAAGTG ATCAGCCCGC CTCGGCCTCC CAAAGTGCTG

GGATTACAGG CGTGAGCCAT CACTTCTGGC CCTTATTCGC ATACAATTTA AAAATCATCA

FIGURE 16 (112)

CAGAAGGTTT GAAAGAAGGA AGGGGCAGAA AATTACCTAC TTTTCCTCTC CCCAGCGATC

TCCTTCAAAT CTGTGCCTTT TCCTCAGGCC CAGGCCTCAA TTTACTGAGC AGTCACACCT

CACAGAGGGA GGTCTGGGCA ATCCACTCTT GGTCACAGGA AAGCCATTGA CCCTCCCACT

TCCTCTCCTC CACCTTGTTC TCAACTCTTG ACTTTGGGCT TTGTTTCTGT TCAAGTCCTA

GGAACTGGTT TCTTTTATCA GGTTAAGTGA TTAGTTCTCT TTCCCTCTAG TTGCTCTCAC

TCCCTGACTC TTGCCTTCTG TAACAACTGG AGACAACTCT TTCAAAACCA GCTCCAAGCC

CCAGACTTCT CTCTGGGCTT TAGTTCGTAA GGCAGGTGCC CTACTGAGTG AGCCTAGATC

AGACAGAAAC ATAGCTGTTG GCAATGATTT AGGTGAATTT CCTTCCATTG TTTTTCTAAT

ACCTTCTTTT TTTTGTAAAT ATAACCATGC ACATACACAC ATATTTGAAT ATCCTGCCTT

TTTATTTAAA ATGACAATAG GTCCGGGAGT GGTGGCTCAT GCCTGTAATC CCAGCACTTT

GGGAGGCCGA GGTGGGCAAT CACCTGAGGT CAGGAGTTCG AGACCAGCCT GGCCAACATG

FIGURE 16 (113)

GTGAAACTCC ATCTCTACTA AAAATCAAAA ATTAGCCGGG CATGGTGGCA GGCTCCCAGC

TACTCAGGAG GCTGAGATGT GAAAATCGCT TGAACCCGGG AGGTAGAGGT TGCAGTGAGC

TGAGATCTTG CCATTGCACT CCAACCTGGG CAATAAGAGC GAAACTCCAT CTCATGGAAA

AAAAAAAAAA AAAGACAGGA TAAACATTCT AGATAGTCTC TATAATGGTC ATGATTAAGA

CAATAAAATA GTCTGAAATT GTCAATATAT ATTAATAATA ATTTATTTGG CCATTCTGCC

AAGTAGCAGA CACCTGTCAT TCTGCCCACT CAGCACCTCT CTTTCTTTTA GGGAAATGCT

ACCCACTCTT TGCATGGGTT CTGGATGGAA CTGTTGATCA CAGTGTTTTC ACTCCCCATT

TTGCCTCACC AGAGGTAGAC AGAAGACCCA AGCCAGGCCA GTTACACACA ATCTTCAGAT

AATTACCGTA TTGATCACAG TATCACCCCA CTCAAGGCTT GGTTGGAGAT GAGCAGAAGA

GACTAAAGCT GGGTCATTTT AATTAACACC TGTACCCCAA AGAAAGACTG TCAATGAGGC

TTTTATACCG ACACTCCTGG TTTCCATTCT TCCTGATGCC ATTCATTTGA CGAACTACCC

FIGURE 16 (114)

AATCTTTCCA ACAGTGTCTT TGGAAGAAAG ATAGTCAGAA AAGAAGATAG AGTTGTTTTC

TGTTCTTTGC AACCAAGGAA CTCTAAATGA TAGACTTGTT GCTAGGCACT TTGGTTATTT

TTATTATCTT GAATACTTCT GTGATATACT TCTTTGTGCA TGCCTGTTTG TACGGATGTA

GCTTTTTATA TATTTTATAT AATTTCTCAG AAGTGGAATT ACTTAGTCAA AAGGTATGAA

CATTTTTCTG ATTCTTAATA TAAATTGTGC AAATGCTTTT TAAGAGGATT ATACCAGTTT

ACATTTTGTG TTATATATAA CAGAAAGTAC TACTGAAAAA ATATTACAAA AATTTGTCTC

TCTGTTCAGG AGGACCTTGT AATAGATGAT AAAGTACTTG AAATAGGAAC ATAGAGCATT

TTCAGTTTAA AATAATTTCA TTGGGTTATT TACGGAATCC TTAGAATTAT GGCCAGACAT

TTATAGATGA TCTGTACCAA ACCTAGGTTG GTTACATAAA TTGCTTATTC AACTGGCTTA

AATCTATAAT AGAAAGATGA CACTTACTGA ATGTTTAATA TACACTTTGT CAGGGGCTTT

GTATTATTCT ATGACATCTT CAAAATGACC CTACTTTCCT ATTTTATAAG TAAGGACAGG

FIGURE 16 (115)

AAGGCTTCAA GAACATGACT AATTTTCCCA AGGGCTGTAC CAAAGCCAGA ACCCAAATCT

ATAAGGCTTT TAAACCTGCA TTCTAAAACT GCATCTCGGC CATCTTATTC CTACAGAACT

TAAGGTTAGA AAGCCAGATT GGAGTCCCAA TTTCACCACT TAGTAACCAG ACAAACTTGA

GGAATTCACT CAACGTCTTT GAATCTTCAT TTTCTAATCT TTAAAACTAA AACAATAATA

CTTGCTCTAC CTATGTCCTA AGATTTCGTG AGGCACATAG AGATAGTGTG GAAGAGTGCT

GTACAGATGT CAAGTGTTAG CGTGATTACT TAGATCCCTG AACACCATGG ATGAATGTCT

CTGACTGCTA TTAGAGGTCA TAAAGAATAT TGGGGCCAGG TACATTGGCT TATTCCTATA

ATGCCAGCAC TTTGGGAGCC TGAGACAGGA GGATCACTCG AGGCCACGAG TTCAAGACCG

GCCTGGGCAA CATAGTGAGA CCCCTTCTCT ACAAAAAAAA AAGCAGCCAC GTGTAGTGGC

ACACACCTGT AGTCCCACAT ACTCAGGAGG GTGAGTTGGG AGGATAACTT TAGTCCAGGA

GTTTCAAGGT GCAGTGAGCT GTGATTGCAC CACTGTACTC TAACCTGGAC AGCAGAGTGA

FIGURE 16 (116)

GACCCTGTCT CTAAAAAAAA AGAAAAAAAA ATAATAATAA TAAAGAATAA TGGGGCCTTG

GGATACCCAC TCCTCTCTTT CTGCTCTGAG TTGTGAAGCA GTTGAGTTAC ATATGCATGT

CCAATGGATG AGGTTGAAAA TATCAACTGG ATTGGAATGT GGCTTACTTG CGTGGCCACA

ATGAGCTTCG TAACACTTCC TGACAGGGTG AGAAGACAAA CTTCCTCACC CAGTCACTGG

CAGAGCTGGA CACTCTGTGT CTCTCCCACA GAACAACCTC TTACTGCATG GAGGTGGATG

AAAAAGTCAA CCGAGAACAG GCTACTCCAA AAAGCAGAGC ACCAAAGGCA CCAGCTGGTC

AGGTCCCCCT TCCTAAGTAA ACAATCACGT AATTCATTCG GGACAAAGCC AGAGAGGTGG

TGTGGAGAAA GAGAGGGCAG TTTCCTCCCA AGTTTTTCCT GGAATTCTTT ATGGGAATAT

GAGGTTTAGG GGAATAAGAC TTCCCTTTAA CAGTGAAGAA TCCCCAGCTC TATTGGTAAT

AGGAAATCGC TTACAAGGAT CATGGGGAGT ATTTCCTCAG CTCGTTCTGC CTCCTACTTG

GCTGAGTGGA ATGGAACCAT CTGTGGCTGC TGCATATGAT ATTGTCAACT TTGTCATTCC

FIGURE 16 (117)

ACACCCACTC CTTGACGCCC TACCATGTGG TCATAAGACT CCCTTTAAAG TGTTCCTTTA

AAAAACAAAA TGTGTTTTGT TTCTATAAAA TACAGCTCAA TGTCAGAACC CTTGTCTTGT

TTGCTCTCTG ATGTAACCCT TTCACAATGT TTGGGCAGCT TATTCTCTCT ATTTCCCTGT

AGGGTCCCAT CCAGGCCAAA GTGAGTGCCA GCCTCATTTG GGCAGCAGAT GCCCTGTGGA

AGGGCAGGAG GAGACGAGAG CTAATTGTAA CTTTGTGATT AGCTGTCATG GATGCCTGGT

CCTGTCAATA GCGCTCAATA AAGCCAGAAG GCCAAGCGTT CGCTTCTGCA TACTGATTGC

TGAGTCAGAT TTCTCAGTGC AGAAGGGCTT TCTAGGCAGT CAATTTTAGA ATATTAGTCT

TGGTTCTTAA GTGGTTAAAA TCCCTAGCTG GTCTTTAATC TGAGCCTGGA GAATTTAGTT

ATGGCTGACA TTCTGCTGTG ATATTTTTGC CCTCAATATA TATGTCTTTC CTCCATCTCT

TAGATCCCTG AATCATAGAG ATATATATGT TATATAATCA ACTGTCTCCA GTCTCTAAGA

GTGATAAGTA CACATTGTGT CAGGTTGAGG GGACAGGAGA ACTTTCAAAA GCCTTTCTTG

FIGURE 16 (118)

CCCCTTTTTC CTTCTCACTG CCTCCCACTA AGTCCAGCCA CTTATTATTC AGCTGACACT

ATCATCATGA CCATGAGGTC TTTTGGGGCT ACCCTGGTTC GGATCCTTCT GGAGGTTTGT

TGCTTAACTC TGTCTTCAGT CCTATGAGCT GCTTTTTCAA TAAGTTTCTA TTTTGGCTAA

AGTTGGCCAG AATCTCCTTG TAACCAAAGA ACAAATAAAA TACCAGCTTG CAATGTTCTA

TGTTGCTTCC ACCAAACTTA TGCAGCACTT CCTATCTAAT CCACCTACTA GTCTTTTTTT

TTTTTATTTT TTTTGAGACG GAGTCTCGCT CTGTTGCTCA GGATGGAGTG CAATGGTGCA

ATCTCGGCTC ACTGCAACCT CTGCCTCCCG GGTTCAAGCA ATTCCCCGGC CTCAGCCTCC

TGAGTAGCTG GGACTACAGG TGCATGCCAC CACGTCCGGC TAATTTTTGT ATTTTAGGAG

AGAGAGGGTT TCACCATGTT GCCCAGGCTG GTCACGAACT CCTGAGCTCA GGCAATCCGC

CCTCCTCGGG CTCCCAAAGT GCTGGGATTA CAGGAGTGAG CCACCTCACC TGGCCCCGAC

CTACTAGTCT TTAGTGTTTG CTTCCTTCTA TTGGGTAATT GTCTGTTTAT ATGCATGTCT

FIGURE 16 (119)

TGTTTCCTCA AATAAAATGT GGTCTTCTCA AGGGTATTGG CCCATGTTCT ATCCATCTGT

AGATATCACA GCACCTAGCA GTGTCTTTCA CAGAGGAAGT ACACAACTGG CATTATTGAT

TCATTGCTCC ATTTTTTCCT TCTTTATCCC CAGCATTTCT CAATAATTTC AAACATCTCC

ATTGGAGTAC CGGAGAAAGC AGGTAGCTTT ACTTGCAGCT ATGTTTCTAT CCCCATAGTA

ACTAAAAGAG GACCCAGAGA AACATGTTTA AATGCTGTCC TGTTATCAGG ACCTCAGCCT

TCTGATGCTC CGTGGCTTGG GGGTTATTGC TTGATCATCT CCTCCCCAAC CTACACTGTG

TACCTATGCT AGTCTCTTCA TGAGGACTAA GCCCCATAGT AAAAGGGCTA GATAAATAGA

AAATCATTTT ATGTAATTAT AAGAATGAGA ATACTGAGTA TTCTGGTGTT TGTTTAGGAT

AAGCACATCT TTATTTGTAT GAGAAAAAGA AAAAGAGAGT GAAAAATATA TTAACGTGCA

TATTGTTCAG AACCCTTGGA TTGCAAGTGA CAGAAACTCA ATTCAAACCA ACGTAAGTCA

AAAGGAAAAT ATATTGGCTC ATGTAACCTT CTCACAGAGA GGGCAGGATG GAAGGGGCTT

FIGURE 16 (120)

TGGGAACAAG AGAATTGTTC TCAAATTCTA GGAATACTAG GATTAGTCCA GGATGGGTCA

CCTTCCTGTC CCTGAGGTGG TGGTAGCGAT GGTAGAGTCT TATGGGAGGA AAGAGTGCAT

GTTAGGATGA AGGTAGGGCT AAGCAAACAA GGGCAAGGGC CACTATATCA TGCTAAAAAT

GGTTTTTTTT GATGTCTTCC TTAATTTCAC AAATGCTTCC AACAAAGTAG CACACAGGAA

AAAGAACATA GGGACTCTAC TGGTGGGTGC TTTTATCTTA AGCCTTGTAC TTGCTTTTCA

CAGCTTACTC ACTGCTTGTA CCTGAGGCCA TATGCCCTGT AAAAGCTTCT GCAGGGTTTC

TACTAAGCTG GGTTCCTTAT ATGGCTCTCT CCCATTTCTG TTGCCTCACT CTAGTGATCT

TTCTCTTTTC CTCACCTCTG GGACTGGTGG CTGTTTGTAT GGACTGCCTT AGCTTTGCTT

TGGGTTTTTT CCTGGGGACA ATGTCTTCAG ATTATCCTAG ACCAAATAAA CTACAGCCAC

TGGGCCAGGC TCTTCCTCCT CCAACTGGAC CATGTTCCCA GGGCTCTTCA CCTTAGTTTA

GGTCAAGCAT TCTTGGCAAA AGAAAGGCCT AGTTAACAAT AGACATTCTA GCAATTGATT

FIGURE 16 (121)

CTTTTTGACA TGTTGTAAGA TCTATTCACA TTTTGTAATT AAAGCATTCC CCTATGGAAA

CCAACACGAA CTAAGCTGCT CCTGGAATGC AGGGTGGCCT CCTCAATACA GGATGTTCTA

GAGAGCTGTA TTTTGGGCAC TTAACTATTC TCCACTACTT AGGGCACAGC ACTGAAATTA

ACACCACTAA GTTTGTCATG TCCATGTAGT TAGTCTCAGG CAGTGCAGCC TCAGGAGTGG

AACTGACCTC TTATGTGTGT CCAGCCTTTC TTCCTTCAGA AGTCAGCTGT GTTTTCTGCT

GACTCTCCAT AGGAACATCA GTCCTGAATC CTCAGACCAC CATCTGGAGT AGTAAGTGCT

CCTGACAGTC CTAGAAGTTG TCTACCGCTG GATCTCCAAA GCGTGTGACA CACCGTGAGA

GAGAAATGAG AAAGCTGGGC TCTTCAGGTA AATCTTGCTT TTTCACAAGC CCCCTAATTT

TACTGCATAA TTATTTTGAA TTCACTGATA ATTTCTACAA TTTTCCCATA AGTCATCTAC

ACACAATACC CTCTCATGCA ACACTTGGCT TTGCTAATAC ATATCTATTA TGAGAGCTGT

GCTTCTTAAG CGTAAATGTT TTATATGCAC TAAGGCTCTT GGCTTACATA TAAAAGGGGT

FIGURE 16 (122)

ATTGAGCAAT GTGATACAGA AGTCTTTTCT CCACAGGTCT CATATGTAAA GAATTCATTA

GATTGGCTGA AATAGACTGA TCTGTCCATT TCTCTGCTCA CTTATCATAA GGAAGTCATT

AGCTAAGGAA CAAAAACTAC AATCTATGTA ATTAGAAGAA CAAGCTGGTT TTGCTCAATA

TAAAAATAAG AAAAAGAAAC CATGTGAAAG TCAAAATATT TGTTTAATCA GGTCATTGAG

AATCTATTAA AAAGTATTTG AATTCTTTAT GATGAGAACT ATCTTGACTC AAGTGGACAG

TGGTGAGCTT TTTGGCCTGT GGTCCCTACG TAGAAAGGAG GCTTTGTCAT AAAGTCTTAT

ATGGTACAGG TGCCAAGTTA AGTGCCCAAG CTTGCTCTTA AAAGCATACT GGATTTTG

INTERNATIONAL SEARCH REPORT

International Application No.
PCT/AU 98/00352

A.	CLASSIFICATION OF SUBJECT MATTER
Int Cl^{6}:	C12N 15/11, 15/79 A61K 48/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
WPAT (see below) STN (CA - see below)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
MEDLINE (see below)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
WPAT - (ARTIFICIAL CHROMOSOME# OR MINICHROMOSOME# OR MINI CHROMOSOME# OR MICRO CHROMOSOME# OR MICRO CHROMOSOME# OR YAC# OR MAC# OR HAC# OR CENTROMERE# OR NEO CENROMERE#) AND C12N-015/IC

STN (CA and MEDLINE): CENTROMERE AND (ALPHA SATELLITE OR ALPHASATELLITE)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
PX	Human Molecular Genetics 6(8), pages 1195-1204 (1997) Depinet, T.T. et al "Characterization of neocentromeres in marker chromosomes lacking detectable alpha-satellite DNA." See whole document.	1-4, 11-17, 24-30, 37-39, 61-64, 71-74
PX	Genetic Counseling 8(4), pages 341-343 (1997) Petit, P. and Fryns, J.P. "Interstitial deletion 2P accompanied by marker chromosome formation of the deleted segment resulting in a stable acentric marker chromosome." See whole document.	1-39, 61-74

[X] Further documents are listed in the continuation of Box C

[ ] See patent family annex

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier document but published on or after the international filing date
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"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
7 July 1998	14 JUL 1998
Name and mailing address of the ISA/AU AUSTRALIAN PATENT OFFICE PO BOX 200 WODEN ACT 2606 AUSTRALIA Facsimile No.: (02) 6285 3929	Authorized officer JIM CHAN Telephone No.: (02) 6283 2340

INTERNATIONAL SEARCH REPORT

International Application No.
PCT/AU 98/00352

C (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
PX	Nature Genetics 16(2), pages 144-53 (1997) du Sart, D. et al "A functional neo-centromere formed through activation of a latent human centromere and consisting of non-alpha-satellite DNA." See whole document.	1-39, 61-74
X	Human Genetics 97, pages 453-6 (1996) Bukvic N. et al "An unusual dicentric Y chromosome with a functional centromere with no detectable alpha-stellite." See whole document.	1-4, 11-17, 24-30, 37-39, 61-64, 71-74
X	Cancer Genetics & Cytogenetics 39(1) pages 1-6 (1996) Abeliovich, D. et al "dup (109) lacking α-satellite DNA in bone marrow cells of patient with acute myeloid leukemia." See whole document.	1-6, 8-19, 21-32, 34-39, 61-66, 68-74
X	Proc. Natl. Acad. Sci. USA 93, pages 8512-17 (1996) Dawe, R.K. and Carde, W.Z. "Induction of centromeric activity in maize *suppressor of meoitic drive 1*." See introduction and discussion.	1, 2, 15, 16, 61, 62
X	Trends In Genetics 11(9) pages 337-9 (1995) Brown, W. and Tyler-Smith, C. "Centromere Activation." See whole document.	1-74
X	Am. J. Human. Genet. 54, pages 877-83 (1994) Blennow, E. et al "Tetrasomy 15q: Two marker chromosomes with no detectable alpha-satellite DNA." See whole document.	1-4, 11-17, 24-30, 37-39, 61-64, 71-74
X	Am. J. Human. Genet. 55, pages 1202-8 (1994) Ohashi, H. et al "A stable acentric marker chromosome; possible existence of intercalary ancient centromere at distal 8p." See whole document	1-4, 11-17, 24-30, 37-39, 61-64, 71-74
X	Am. J. Human. Genet. 52 pages 1153-63 (1994) Voullaire, L. E. et al "A functional marker centromere with no detectable alpha-satellite III or CENP-B protein: activation of a latent centromere?" See whole document.	1-39, 61-74
A	WO A 97 16533 (THE REGENTS OF THE UNIVERSITY OF CLAIFORNIA) 9 May 1997. See whole document.	1-74

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No.
PCT/AU 98/00352

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report		Patent Family Member	
WO	9716533	US	9716533

END OF ANNEX